Occupational Exposure to Dibutyl Phthalate Among Manicurists

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Objective: *To measure manicurists' exposure to dibutyl phthalate (DBP) at work and to determine whether workplace characteristics influence this exposure. DBP is a reproductive and developmental toxicant in rats and is used in nail polish to hold color and prevent chipping.* ***Methods:*** *Pre- and postshift spot urine samples were collected from 40 manicurists. Linear regression compared the relationship between the log of the cross-shift differences in urinary phthalate monoester metabolite concentrations and use of workplace exposure control methods.* ***Results:*** *There was a statistically significant cross-shift increase of 17.4 ng/mL in the urinary concentration of mono-n-butyl phthalate, the major metabolite of DBP. Use of gloves reduced mono-n-butyl phthalate concentrations by 15.1 ng/mL below the preshift concentration compared with a 20.5 ng/mL increase if gloves were not worn.* ***Conclusions:*** *Manicurists are occupationally exposed to DBP and glove use may minimize this exposure.* (J Occup Environ Med. *2008; 50:705–711*)

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Phthalates are a class of man-made chemicals widely used to soften plastics, act as adhesives or solvents, and hold color and scent in consumer and personal care products. Phthalates can be found in paints, flooring, wall coverings, carpets, glues, printing inks, insect repellents, hair spray, shampoo, nail polish, cosmetics, medications, and medical intravenous bags and tubing made with polyvinyl chloride (PVC).[1–5] Dibutyl phthalate (DBP) is a common ingredient in nail enamel and polishes. DBP was found in 67% of nail polishes examined in the United States[6,7] and 90% of nail polishes examined in Korea.[8] One brand of nail enamel was reported to contain DBP at a concentration of 59,815 parts per million.[5]

As there are many potential sources of phthalates in the environment, the magnitude of specific exposure routes has yet to be quantified.[9] Food has been hypothesized to be the primary exposure route for some phthalates but not for DBP.[10] Inhalation[11] and dermal exposures can be important routes for DBP[12] exposure in the general population and in the workplace.[13]

Occupational DBP exposure may occur among manicurists likely via both inhalation and dermal absorption due to work practices and nail products. Nationally there are 333,000 licensed manicurists, 12,000 of whom are licensed in the State of Massachusetts.[14,15] A national survey of manicurists reveal that most are women (96%) of childbearing age (mean age is 38 years), 41% are White, and 38% are Vietnamese.[16] Average income is estimated to be

$32,000 nationally.[16] Nail salons have been evaluated for other hazards such as ethyl acetate, n-butyl acetate, toluene, acetone, and ethyl methacrylate; nevertheless, to date no studies have measured exposures to phthalates.[17,18]

After exposure, phthalates are metabolized; the metabolites are generally excreted within 24 hours and completely eliminated in 48 hours.[2] Despite rapid elimination, phthalate metabolites are detected in urine samples from the general population and can serve as biomarkers for phthalate exposure.[4,19,20] These phthalate metabolites are shown to be the active toxic species.[21] Specifically, animal studies clearly demonstrate adverse developmental and reproductive effects from several phthalates, including DBP.[22–30]

Few studies have investigated the human health effects of occupational exposure to DBP. Urinary phthalate metabolite and reproductive hormone concentrations in 74 exposed men who worked in PVC production were compared with concentrations in 63 unexposed male construction workers. Exposed men had significantly higher mono-n-butyl phthalate (MBP) and mono-2-ethylhexyl phthalate urinary concentrations. Exposed men also had significantly lower concentrations of serum-free testosterone when compared with controls.[13] No occupational studies of women exposed to DBP were found.

General population level exposures to phthalates have shown inverse associations between urinary concentrations of MBP, the main metabolite of DBP, and semen quality.[31–33] Swan et al[33] reported an association between elevated third-trimester maternal urinary concentrations of monoethyl phthalate, monoisobutyl phthalate (MiBP), MBP, and monobenzyl phthalate and decreased anogenital distance in male infants.

The primary objectives of this study were to quantify nail salon workers' occupational exposure to DBP, identify workplace characteristics that may influence urinary phthalate metabolite concentrations, and determine the effectiveness of local exhaust ventilation, masks, and glove use in reducing occupational phthalate exposure.

Materials and Methods

Design and Setting

The Institutional Review Board at the Harvard School of Public Health and Simmons College approved the study. All participants gave written informed consent. Subjects were recruited from a local health center, beauty academies, nail technology schools, and nail salons in Boston and surrounding areas. Recruitment was conducted from January 2004 to November 2005 by means of personal invitation, distribution of flyers, referrals, personal contact with nail salons or schools, and nail product distributors. Manicurists under the age of 18 were excluded.

Demographics and Working Environment

Self-administered questionnaires were used to collect demographic information such as gender, height, weight, race, country of birth, and smoking status. Work-related questions included the number of hours worked, number of manicures completed per shift, the presence of exhaust ventilation, or open windows or doors on the day of specimen collection. In addition, manicurists were asked whether they wore masks or gloves during work, whether they ate in the salon, and the number of clients frequenting the shop each week.

Urinary Phthalate Monoester Measurements

On a single workday for each manicurist, pre- and postshift urine samples were obtained. Most manicurists complied with instructions to collect both urine samples on the day after a scheduled day off from work. Subjects were instructed to collect the samples in a sterile urine collection cup (prescreened for phthalates) at home before leaving for work (preshift) and after work (postshift) and to freeze the samples immediately after collection. Frozen samples were placed in a Styrofoam container on ice packs and delivered directly to the laboratory at the Harvard School of Public Health and stored at −20°C. When recruitment was complete, the samples were thawed, analyzed for specific gravity with a handheld refractometer (National Instrument Company Inc., Baltimore, MD), aliquoted for either storage or for analysis, refrozen, and shipped on dry ice to the Centers for Disease Control and Prevention (CDC) (Atlanta, GA). Unpublished analyses of repeated freeze-thaw cycles of samples from this study revealed that metabolites of DBP were remarkably stable over the course of 2 or more years. There are several ways to adjust for urine volume.[34,35] Although creatinine is a frequently used form of adjustment, if a compound is excreted primarily by tubular secretion such as organic compounds that are conjugated by glucuronides in the liver (which phthalates are), it is not appropriate to use a creatinine adjustment.[34,35] Therefore, we used specific gravity to normalize phthalate concentrations for urinary dilution.

For the primary objective of the study, occupational exposure to DBP (commonly found in nail polish), we present data on only MBP, the main metabolite of DBP, and mono-3-carboxypropyl phthalate (MCPP), an oxidative metabolite of DBP, and MiBP, a metabolite of di-iso-butyl phthalate, a structural isomer of DBP. Analytical methods have been described in detail elsewhere.[36,37] Briefly, analysis involved enzymatic hydrolysis of phthalate metabolite conjugates, preconcentration with solid phase extraction, high performance liquid chromatography (HPLC) separation, and detection by isotope-dilution tandem mass spectrometry. Limits of detection (LODs) were ~1 ng/mL or less for all phthalate metabolites.

Statistical Methods

All analyses were performed using SPSS (Version 14) for Windows. Phthalate concentration data were explored for normality and log transformed. Urinary phthalate monoester concentrations were adjusted for dilution by specific gravity using the following formula: $P_c = P[(1.024 - 1)/SG - 1]$. P_c refers to urinary phthalate concentration adjusted for specific gravity, P is the measured phthalate concentration (ng/mL), and SG refers to specific gravity. For urinary phthalate concentrations that were below the LOD, a value equal to half the LOD was imputed.

For each individual, a cross-shift change in the specific gravity adjusted MBP, MiBP, and MCPP metabolite concentration was calculated as the difference between the after-work and before-work concentrations. The Wilcoxon signed rank test was used to determine if the individual cross-shift changes in urinary MBP concentrations were different from zero. Linear regression models were used to investigate associations between the individual cross-shift changes in the log of the urinary specific gravity-adjusted monoester phthalate concentrations and potential work environment predictors, such as presence of local exhaust (yes/no), open windows or doors (yes/no), use of masks and gloves (yes/no), and eating in the workplace (yes/no).

After evaluating appropriateness using quadratic terms, age and body mass index (kg/m^2) were modeled as continuous independent variables. Smoking status was categorized as current smoker and current nonsmoker (includes ex-smokers and never smokers). Race and ethnicity were collapsed into two groups; Asian and the reference group of non-Asians. Exhaust ventilation was defined as the self-reported use of a local exhaust unit at the manicurists' workstation which exhausted directly to an outside source (0 = no table exhaust used, 1 = table exhaust used on the day of urine collection). Gloves and mask use, general ventilation (determined by two self-reported variables: windows or doors open on the day of specimen collection), and eating status were dummy coded (0 = no, 1 = yes). The variables, total number of hours worked, and number of nail treatments performed on the day of specimen collection were also evaluated as potential confounders. Stepwise multiple linear regression analysis was performed to determine which of the above independent variables were important in determining cross-shift changes. The significance level for entry and inclusion in the model were $P < 0.05$ and $P < 0.10$, respectively.

Results

Subject Demographics

Of the 40 manicurists recruited for this study (from about 80 salons approached, a beauty academy, and a health center), two manicurists did not provide written survey data, and three did not provide postshift urine samples. Therefore, survey data for 38 manicurists were included in the descriptive analysis and 37 manicurists were included in the cross-shift analyses. The study population was comprised mainly of White (47%) and Asian (42%) manicurists with 11% of other ethnicity. Only four of the participants were men. The average age of participants was 35.8 years. The majority of the subjects were born either in the United States (47%) or in Vietnam (37%). Seventy-eight percent of participants reported being current nonsmokers (Table 1).

Work Environment Characteristics

The average hours worked on the day of participation was 7.4 (standard deviation [SD] = 2.3) and the average number of treatments (ie, manicures, pedicures, acrylics) performed that day was 6.4 (SD = 3.9). Manicurists reported that windows and doors were open in 30% and 46% of salons, respectively on the day of urine collection, whereas local table exhaust was used in 22% of salons. Of the participants, 41% reported wearing a paper mask, 22% reported wearing gloves during work, and 76% ate in the salon. None of the subjects reported smoking within the salon (Table 2).

Salon Characteristics

Salons were described by participants as primarily small, family owned and operated (75%) businesses serving less than 50 clients per week (42%), and staffed predominantly with women (90%) employees.

Urinary Phthalate Monoester Concentration Distribution

In all 40 manicurists recruited for this study, we found detectable concentrations of MBP and MiBP at baseline (before work) and MCPP in 95% of these samples. MBP was the

TABLE 1
Characteristics of Study Subjects ($N = 40$)

Characteristic	Mean (SD)	*N* (%)
Age	35.8 (10.2)	
BMI	22.9 (4.4)	
Race/ethnicity*		
Asian		16 (42)
Other (18 White and 2 Venezuelans, 1 NH black, 1 Hispanic Black)		22 (58)
Smoking†		
Current smoker		8 (22)
Nonsmoker (ex- and never smoker)		29 (78)

Percents may not add up to 100 due to missing data.
N indicates number of subjects; SD, standard deviation.
*Race data missing for 2 subjects.
†Smoking data missing for 3 subjects.

TABLE 2
Working Conditions on Day of Participation (N = 40)

Characteristic	Mean (SD)	N (%)
Hours worked on day of study*	7.4 (2.3)	
Number of nail treatments on day of study†	6.4 (3.9)	
Ventilation on day of study‡		
Windows open?		11 (30)
Doors open?		17 (46)
Exhaust used?		8 (22)
Mask worn on day of study§		15 (41)
Eat in salon¶		28 (76)
Smoke in salon‖		0
Gloves worn on day of study#		8 (24)

N indicates number of subjects; SD, standard deviation.
*Hours worked missing on 3 people.
†Sum of treatments missing on 2 people.
‡Ventilation (windows and door) missing on 3 people and ventilation (exhaust) missing on 4 people.
§Mask use missing on 3 people.
¶Eat in salon missing on 3 people.
‖Smoke in salon missing on 3 people.
#Glove use missing on 4 people.

metabolite found in the highest concentration, followed by MiBP, then MCPP. Distribution of before and after work urinary concentrations of phthalate monoesters are displayed in Table 3 for the entire group and for subgroups based on exhaust or glove use. Note that the descriptive statistics in Table 3 show group medians (and 25th, 75th percentiles) and not the median of the cross-shift changes which is what was modeled in the statistical analyses. Glove users had higher MBP concentrations at baseline than those who did not use gloves.

Cross-Shift Analyses

There was a significant increase (17.4 ng/mL) in specific gravity-adjusted MBP concentrations across the work shift; P value = 0.05 (Wilcoxon signed rank test) (Table 4). There was a small (0.3 ng/mL), but significant (P value = 0.05) cross-shift increase in MCPP, a minor metabolite of DBP.[38] No significant cross-shift changes were noted for MiBP.

In linear regression modeling, the individual cross-shift change in urinary MBP concentrations was not related to the number of nail treatments a manicurist completed on the day the sample was collected (P value = 0.57), total number of hours worked that day (P value = 0.83), whether the doors (P value = 0.21), windows (P value = 0.17), or both doors and windows (P value = 0.17) were open on the day of urine collection. Interestingly, manicurists in salons without local exhaust had a 54% (21.5 ng/mL) increase in urinary MBP concentration across the shift compared with a 7% (1.6 ng/mL) decrease across the shift for those with local exhaust ventilation; this cross-shift change by use of ventilation was not statistically significant (P value = 0.88). Glove use, nevertheless, was associated with a significant reduction in urinary cross-shift MBP concentrations (P value = 0.04). Among manicurists who did not wear gloves at work, the median cross-shift MBP concentration increased 50% (20.5 ng/mL) whereas those reporting glove use experienced a 5% cross-shift decrease (−15.1 ng/mL) (P value for cross-shift change by glove use = 0.04). Note that the before-shift urinary concentrations of MBP were quite variable (Table 3) and this accounts for the differences in magnitude of cross-shift changes in MBP in relation to glove use.

TABLE 3
Before and After Work Distribution of Urinary Levels of Phthalate Monoesters* (ng/mL) in 37 Manicurists

Phthalate Metabolite	Overall Group (N = 37)	Exhaust†		Gloves†	
		No (N = 27)	Yes (N = 8)	No (N = 27)	Yes (N = 7)
Before work‡					
MnBP	58.5 (32.3, 10.7)	64.2 (35.3, 109)	46.2 (30.4, 93.6)	42.6 (30.4, 99.4)	91.6 (64.2, 109)
MiBP	10.7 (7.3, 14.9)	10.8 (7.2, 14.4)	9.7 (6.7, 15.7)	10.7 (7.2, 13.5)	10.3 (7.4, 20.2)
MCPP	4.3 (2.6, 6.4)	4.3 (2.2, 5.8)	5.1 (3.1, 8.6)	4.8 (2.5, 6.9)	4.0 (3.1, 6.2)
After work‡					
MnBP	87.2 (33.8, 160)	105.6 (50, 159)	53.7 (22.0, 193)	87.2 (37.9, 149)	69.9 (19.4, 256)
MiBP	10.5 (5.8, 17.3)	10.5 (6.5, 18.6)	9.1 (4.4, 17.0)	10.5 (5.8, 15.9)	7.4 (3.2, 20.2)
MCPP	4.5 (2.2, 8.8)	4.5 (2.0, 8.5)	4.5 (2.3, 16.9)	4.5 (2.2, 8.5)	4.6 (2.5, 9.1)

MnBP indicates mono-n-butyl phthalate; MiBP, monoisobutyl phthalate; MBzP, monobenzyl phthalate; N, number.
LOD (ng/mL) as follows; MCPP, 0.16; MBP, 0.4; and MiBP, 0.26.
*Specific gravity adjusted.
†Missing exhaust on 2 people and gloves on 3 people.
‡Values are group medians (25th, 75th percentile).

TABLE 4
Influence of Local Exhaust Ventilation and Glove Use on Individual Cross Shift Changes in Specific Gravity Adjusted Urinary Phthalate Monoester Concentration (ng/mL Urine)

		Subanalysis by Exhaust[b] (%)		Subanalysis by Glove Use[b] (%)	
Phthalate	Cross Shift Change[a]	No Exhaust ($N = 27$)	Exhaust ($N = 8$)	No Gloves ($N = 27$)	Gloves ($N = 7$)
MBP	17.4 (49%)*	54	−7	50*	−5*
MiBP	−0.6 (−15%)	12	−30	6	−15
MCPP	0.3 (11%)*	11	15	8	14

MBP indicates monobutyl phthalate; MiBP, mono-iso-butyl phthalate; MCPP, mono-3-carboxypropyl phthalate.
**P* value <0.05.
[a]Values are medians of individual cross shift changes and (median of the percent change across the work shift).
[b]Values represent the median of the % change from individual pre-shift urinary phthalate concentrations.

No other variable besides gloves, met the entry and retention criteria for stepwise regression modeling for MBP. The cross-shift MiBP concentration increased 6% (0.21 ng/mL) among manicurists who did not wear gloves and decreased 15% (−2.9 ng/mL) among manicurists wearing gloves, nevertheless, these findings did not reach statistical significance (Table 4). No associations between cross-shift MCPP concentration and exhaust or glove use were detected.

Discussion

We evaluated the relationship between occupational exposure to DBP and urinary excretion of DBP metabolites and whether engineering controls or personal protective equipment mitigated exposure among manicurists in Boston, MA. We found detectable urinary concentrations of MBP and MiBP in all manicurists recruited for this study and MCPP in 95% of them at baseline (before work). In comparison to one occupational study in China among 74 male PVC workers,[13] MBP concentrations among the manicurists (58.5 ng/mL) were an order of magnitude lower than among the PVC workers (548.4 μg/g creatinine) even though different methods of adjustment for urinary dilution were used so results are not directly comparable.

The unadjusted before-work urinary phthalate concentrations from this study (not shown in tables) can be compared with the 2001 to 2002 National Health and Nutrition Examination Survey (NHANES) concentrations reported in the CDC's 3rd National Report on Human Exposure to Environmental Chemicals. Median MBP and MiBP concentrations were 1.6 and 2.4 times higher among manicurists, respectively, whereas median MCPP was 17% lower than the value for NHANES women reported for the years 2001 to 2002.[4] The unadjusted before-work median urinary MBP, MiBP, and MCPP concentrations for manicurists was 34.2, 5.9, and 2.5 ng/mL, respectively compared with the median MBP, MiBP, and MCPP for NHANES women at 21.6, 2.5, and 3.0 ng/mL, respectively. Of interest, the urinary concentrations of MBP in this group of manicurists are comparable with those associated with adverse reproductive outcomes in adult men and with developmental outcomes in infant boys exposed during gestation.[31–33]

The decrease of the cross-shift urinary MBP concentration with the use of gloves supports the possibility that dermal absorption may occur among manicurists. Dermal exposure may occur from direct contact with liquid nail polish or from the settling of dust particles created during sanding and buffing nails. This may mean that the influence of dermal absorption of DBP may be underestimated in the general population as well. In a study among men from an infertility clinic in Boston, MA,[12] evidence of dermal absorption was detected specifically for products containing di-2-ethylhexyl phthalate but not for DBP. This may be because products that contain DBP such as nail polish, are not often used by men. Nonetheless, there is evidence that at least some phthalates are absorbed dermally. Studies in rodents show that dermal absorption of DBP is relatively slow with 10% to 12% of the dermal dose excreted in urine daily, with 60% excreted after 1 week. One week after the application, 33% of the dose was still present at the application site.[39]

Other potential routes of exposure are ingestion and inhalation. Eating in the workplace did not show significant differences in urinary MBP concentrations, which along with the finding of Koch et al,[10] speaks to the fact that ingestion is not a likely source of DBP exposure in this group. Although not statistically significant, manicurists in salons without local exhaust ventilation had a 54% increase in urinary cross-shift MBP concentration, as compared with a 7% decrease for exhaust ventilation users. Further exploration of exhaust ventilation is needed because this analysis was underpowered and there was wide variability in cross-shift changes in urinary MBP.

Several studies have described the intra- and interindividual variability of urinary phthalate metabolites from day to day or month to month[40–42] but not multiple samples within the same day. Two consecutive first morning urine samples were found to be quite similar (intraclass correlation coefficient (ICC) 0.61 unadjusted and 0.80 creatinine adjusted) in a study of 46 African-American women[40] whereas in a study of 27 women and 23 men who collected urine for 8 consecutive days, the ICC was only 0.32 to 0.45 unadjusted and creatinine adjusted, respectively.[41] Although Fromme et al suggests that exposure assessment should not be based on a single urine sample, this recommendation is based on day-to-day variability, not same day data.[41] Without additional information on within-day variation, the within-subject variation in this study is hypothesized to be the result of workplace exposures. The half-life of DBP is short and therefore without additional workplace DBP exposure, the concentration of MBP in the morning sample, which may reflect exposure from personal care products used in the shower, should decrease as the day progressed because there was no evidence of ingestion of DBP in this study. This did not occur, and in fact concentrations rose and this elevation was mitigated in those who wore gloves. It is also possible that glove use could be a marker for safer work behavior like keeping covers on polishes and solvents in the workplace, which would also minimize inhalation exposures. Additional studies are needed to confirm these findings.

This is the first study of phthalate exposure among manicurists, a population typically difficult to recruit. Numerous obstacles exist when recruiting women and minorities in occupational health studies, specifically fear, distrust, lack of knowledge relating to the purpose of informed consent or significance of information that will be used, perceived time constraints away from work or family, subject burden, and transportation and financial costs.[43–46] In fact, halfway through the study, in response to slow recruitment, additional grant monies were obtained to provide a $20 supermarket gift certificate to compensate participants for the time and effort required to complete the study. In addition, focus groups were conducted to determine barriers to recruitment. A small group of manicurists from the greater Boston area were interviewed and found recruitment was difficult because of access issues including lack of privacy in the salon to recruit manicurists without clients overhearing, owner's resistance to allowing researchers into the salons, the busy pace of the salon, and otherwise confirmed themes similar to barriers identified in other studies. Barata et al[45] identified mistrust as a major barrier to participation among minority groups. For manicurists this may be especially important because 70% of nail salon owners and operators in this region are Asian or Vietnamese. The recruitment challenges we identified will require further consideration before any additional studies in this area are conducted. The guidelines recommended in the National Institute of Health's Outreach Notebook for the Inclusion, Recruitment, and Retention of Women and Minority Subjects in Clinical Research[43] may be a helpful starting point.

Conclusions

The present study showed that manicurists are occupationally exposed to DBP. There was a significant cross-shift increase (17.4 ng/mL) in specific gravity-adjusted MBP concentrations (P value = 0.05). Glove use was associated with a significant cross-shift reduction in urinary MBP concentrations (P value = 0.04). Urinary concentrations of MBP, the main DBP metabolite, similar to those found in this study have been associated with reproductive outcomes in men and developmental outcomes in male infants exposed prenatally.[31–33] Despite the challenges associated with recruitment, further research is needed among manicurists because they are primarily young women of reproductive age, some of whom may be trying to get pregnant or who are pregnant, and toxicological and limited human data suggest adverse developmental and reproductive health effects of DBP.

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