HHS Public Access

Author manuscript

Int J Hyg Environ Health. Author manuscript; available in PMC 2022 January 01.

Published in final edited form as:

Int J Hyg Environ Health. 2021 January ; 231: 113630. doi:10.1016/j.ijheh.2020.113630.

Assessment of Triphenyl Phosphate (TPhP) Exposure to Nail Salon Workers by Air, Hand Wipe, and Urine Analysis

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Abstract

Triphenyl phosphate (TPP or TPhP) is commonly used as an additive plasticizer or organophosphate flame retardant (OPFR)in consumer products including nail polish. We evaluated exposure to TPhP from 12 nail salon technicians working at four nail salons located in California over a period of two work days. Bulk samples of 15 nail polish and other nail products were collected. Study participants also provided two personal air samples, two hand wipe samples (pre- and post-shift on day two), and two urine samples (pre-shift day one and post-shift day two). The geometric mean (GM) of TPhP air sampling concentrations was 7.39 ng/m^3. Post-shift TPhP hand wipe concentrations (GM 1.35 μg/sample) were significantly higher ($p = 0.024$) than pre-shift hand wipe concentrations (GM 0.29 μg/sample). Diphenyl phosphate (DPP or DPhP), a urinary metabolite of TPhP used in this study as a biomarker of exposure, was detected in all post-shift urine samples and 75% of urine pre-shift samples. DPhP post-shift concentrations (GM 1.35 μg/g creatinine) were significantly higher than pre-shift concentrations (GM 0.84 μg/g creatinine; $p = 0.012$). In addition, DPhP post-shift concentrations were correlated with TPhP post-shift hand wipe concentrations, suggesting dermal contact may be a relevant exposure pathway for nail salon workers.

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Keywords

Plasticizer; Flame retardants; Organophosphate Flame retardants (OPFRs); Nail Salon Workers; TPHP

1. INTRODUCTION

Triphenyl phosphate (TPP or TPhP) is commonly found as an additive plasticizer in personal care products such as nail polish at levels up to 16.8 mg/g (or 1.68% by weight) (Mendelsohn et al., 2016). The increase of TPhP's prevalence in nail polishes can most likely be attributed to the decrease in use of another plasticizer, dibutyl phthalate, due at least in part to pressure from consumer groups (Mendelsohn et al., 2016; Nails Magazine, 2018; NY Department of Public Health, 2016). A recent study found dibutyl phthalate was not added to nail polish (Young et al., 2018). Conversely, TPhP was found in half of the 1,500 nail polishes reported in the Environmental Working Group's cosmetics database (Environmental Working Group). In one study comparing exposure to TPhP by sex women had 84% higher urinary levels of diphenyl phosphate (DPhP), a metabolite of TPhP often used as a biomarker of exposure (Hoffman et al., 2014; Mendelsohn et al., 2016; Craig et al., 2019). These results may be attributed to the difference in personal care product and nail polish use between males and females (Hoffman et al., 2014; Silva et al., 2004). Further, results from recent studies suggest that nail polish can also be an important source of chronic exposure to TPhP for those occupationally exposed (Broadwater and Chiu, 2019; Mendelsohn et al., 2016; Young et al., 2018).

TPhP, in addition to being used as a plasticizer, is one of the most commonly used organophosphorus flame retardants (OPFRs). OPFRs represent a large group of alternative flame retardants that have become more prevalent as they have replaced polybrominated diphenyl ethers (PBDEs) (Van Der Veen and De Boer, 2012). Occupational exposure to OPFRs is not currently well characterized. TPhP is primarily used in polyvinyl chloride (PVC) and polycarbonate/ABS alloy (PC/ABS) plastics, polyurethane foam, hydraulic fluids, photographic film, and nail polish (Marklund et al., 2003; U.S. Department of Health and Human Services, 2011; UK Environment Agency, 2009; World Health Organization, 1991). TPhP can also be readily found in the environment within sediment, soil, dust, and air (He et al., 2016; Salamova et al., 2014; Van Der Veen and De Boer, 2012).

Once absorbed into the body, TPhP is metabolized into DPhP (Van den Eede et al., 2015; Van Den Eede et al., 2013) and has a reported half-life of 9.5 days (Wang et al., 2020). Among the U.S. general population from the National Health and Nutrition Examination Survey (NHANES) 2013–2014, the DPhP geometric mean was 0.904 microgram (μg) per gram creatinine, the 95th percentile was 5.51 μg/g creatinine (Ospina et al., 2018).

There is limited research on the toxic effects of TPhP in human cohorts. In a study on zebrafish, TPhP exposure significantly altered neurotransmitters, γ-aminobutyric and histamine and also inhibited total acetylcholinesterase activity, which is considered a biomarker of neurotoxicant exposure (Shiet al. 2018). Other studies on zebrafish, mice and rats have found evidence of cardiotoxicity, genotoxicity, metabolic disruption and endocrine

disruption from TPhP exposure (Du et al., 2016; Liu et al., 2012; Mendelsohn et al., 2016; Mitchell et al., 2018; Patisaul et al., 2013; Shi et al., 2018; Wang et al., 2018; Zhang et al., 2016).

The recommended occupational exposure limit (OEL) for TPhP in air is 3 mg/m^3 averaged over an eight hour work shift as determined by the Occupational Safety and Health (OSHA) Administration Permissible Exposure Limit (PEL), the National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) and the American Conference of Governmental Industrial Hygienist (ACGIH) Threshold Limit Value (TLV) (NIOSH, 1994; OSHA). The ACGIH TLV was set at this level for possible eye and skin dermatitis and irritation (NCBI, 2005). Since this designation, some occupational exposure assessment studies have been conducted on TPhP. In one study, TPhP levels for indoor air (1.2 ng/m^3) were an order of magnitude higher than outdoor air (Wong et al., 2018). Another exposure assessment of TPhP in office air samples reported a concentration range of 0.25–10.21 ng/m^3 with a mean of 2.09 ng/m^3 (Yang et al., 2014). In an occupational cohort of aircraft maintenance technicians, urinary concentrations of the TPhP metabolite were measured. These workers appear to be chronically exposed to TPhP, as DPhP pre-shift median and post-shift median urine concentrations were 5 and 7-fold higher, respectively than in a control group from the general population (Schindler et al., 2014). In a recent occupational exposure assessment by NIOSH (2018), electronic recycling facility workers provided full-shift personal air and urine samples. The TPhP geometric mean air concentrations was 117 ng/m^3 with a range from non-detectable (< 0.9 ng) to 1,800 ng/m^3. The median DPhP urine concentrations among participants in the electronic shredding area doubled from pre-shift (0.868 μg/g creatinine) to post-shift (1.76 μg/g creatinine) (Beaucham et al., 2018). One study examining occurrence of OPFRs in various air environments found TPhP concentration was higher in a nail salon (43.7 ng/m^3) compared to homes, automobile part shops, and electronic shops (Kim et al., 2019). Another study found that personal air samples collected from nail technicians had lower TPhP concentrations than chemical manufacturing and electronic dismantling workers, and lower hand wipe exposures than chemical manufacturing workers (Estill et al., 2020). Nevertheless, these data suggest nail salon technicians may be occupationally exposed to TPhP.

Although there have been a few exposure assessments for TPhP, there have been limited occupational assessments of nail salon technicians who may be chronically exposed to TPhP in nail polishes. We sought to evaluate exposure levels to TPhP and to identify routes of exposure and exposure determinants among nail salon workers by using measurements in air, hand wipes, and urine samples.

2. METHODS

Four nail salons located in the San Francisco area in California (USA) were recruited in 2016 to participate in this study. All workers on site at each salon were asked to participate and given a brochure regarding the study. Materials were previously translated into Vietnamese and a translator was onsite to answer any questions. Workers signed an informed consent approved by the NIOSH IRB and were monetarily reimbursed for their time. Participants were asked demographic and career-related questions to better understand

their exposures (Table 1). We conducted environmental (i.e., air, bulk samples of nail products, and hand wipes) and biological sampling (i.e., urine) to evaluate two days of exposure for each participant. Sampling was conducted over a two-day period on a Friday and Saturday, generally the busiest days of the week at nail salons.

All nail salons included in this study offered manicures and pedicures. All shops except salon A performed acrylic nails. Salons C and D provided haircuts, hair coloring, and waxing. At each facility, two of the three workers worked the entire time the shop was open. Salon temperature was measured each hour and ranged from 66 to 74°F. Nail technicians were predominantly female, but salon B had male nail technicians.

During the sampling period, an industrial hygienist viewed workers at each salon at least once an hour to evaluate personal protective equipment (PPE) usage. Glove use was categorized as yes, no, and intermittent, as some workers took their gloves on and off for different tasks. Paper or cloth medical mask use was categorized as yes or no. Nail polish worn in the last week was categorized as yes or no.

TPhP was the analyte of interest when evaluating bulk, air, and hand wipe samples. Air and hand wipe samples were also analyzed for tricresyl phosphate (TCP), reported in a previous manuscript (Estill et al., 2020). A metabolite of TPhP, DPhP, was quantified in spot urine samples.

2.1. Bulk Samples

Bulk samples of products potentially containing TPhP were collected from each nail salon. Nail polish and other products including lacquer, base coats, and top coats were sampled at each site. We sampled products that were used by the nail technicians during the day, collecting at least one sample from each nail salon visited. If we had previously collected a bulk sample of a particular brand and type of nail polish, we did not collect another sample. Additionally, we did not sample all colors of the same product. We collected samples from 15 products of which 11 were regular-use polishes.

2.2. Air Samples

Similar to our previous study of spray foam workers, (Estill et al., 2019) all nail technicians wore AirChek 5000 (SKC, Eighty-four, PA) pumps calibrated to a flow rate of 1.0 L/min for use with a custom OVS-2 tube with a glass fiber filter and two XAD-2 sorbent layers with glass wool separators. Sample pumps were worn on a belt with intake connected near the worker’s collar. If workers wore a paper or cloth medical mask, the sample was collected on the outside of the mask. Personal air sampling was conducted during participants’ entire work shift for an average of almost 8 hours per day. All pumps were calibrated before use to within ten percent of the target flow rate and after use using a medium flow DryCal Defender (MesaLabs, Lakewood, CO). Air samples were analyzed for TPhP.

2.3. Hand wipe Samples

Workers provided pre-shift and post-shift hand wipe samples on the second day of sampling. Sample jars were prepared less than a week before sampling. Two 3”x 3” sterile gauze

pads (Dynarex, Orangeburg, NY) were placed in 120 mL amber glass jars (Fisher Scientific, Pittsburgh, PA). In each jar, we pipetted 6 mL of 99% HPLC grade isopropanol (Fisher Scientific). The jars were then tightly sealed and stored at approximately 5°C. Hand wipe samples were collected in a break room before and after the work shift. For sample collection, an industrial hygienist instructed participants to remove gloves, grab one of the gauze pads and wipe both bare hands for 30 seconds. Then they were instructed to grab the other wipe and repeat the process. Both gauze pads were placed back into the jar, sealed, and refrigerated (< 4C) until analyzed. For the post shift hand wipes, workers were asked if they washed their hands since providing the pre shift hand wipe sample. The hand wipe samples were analyzed for TPhP.

2.4. Urine Samples

Workers provided spot urine samples in sterile urine collection cups at the workplace prior to their first-day shift and after their second-day shift. Two urine samples were collected and analyzed for each worker. Participants were instructed to wash their hands with only water and let them air dry before providing a sample. A minimum 60 mL of urine was requested for each worker. Following collection, samples were kept in coolers with ice until aliquoted into 10 mL polypropylene vials and stored at or below −20 °C until analyzed.

2.5. Sample Analysis

Air, hand wipe, and bulk samples were analyzed for TPhP at Virginia Institute of Marine Sciences, College of William and Mary. The analysis was completed by ultra-performance liquid chromatography (UPLC) - atmospheric pressure photoionization (APPI) tandem mass spectrometry adapted from La Guardia and Hale (La Guardia and Hale, 2015).

Urine was analyzed for a panel of OPFR biomarkers at the CDC's National Center for Environmental Health as described by Jayatilaka et al. (Jayatilaka et al., 2017), as part of a larger study examining flame retardant exposures in various industries. However, this manuscript only reports on DPhP (internal standard= d_{10}-DPhP) urinary concentrations which was used as the biomarker of exposure for TPhP, consistent with previous exposure studies (Hoffman et al., 2014; Mendelsohn et al., 2016; Ospina et al., 2018; Craig et al., 2019). Other metabolites of TPhP that were not included in this study because their analytical standards were not commercially available include hydroxyl triphenyl phosphate (OH-TPhP), di OH-TPhP, and MPhP (Su et al., 2015; 2016).

In brief, 400-μL of urine underwent enzymatic hydrolysis of conjugates of the target biomarker β-glucuronidase Type H-1 from Helix pomatia, followed by off-line solid phase extraction, separation via reversed phase high-performance liquid chromatography, and detection by isotope dilution-electrospray ionization tandem mass spectrometry. Results reported here are adjusted for creatinine to account for urine dilution (CDC, 2019).

2.6. Quality Control

A surrogate standard, deuterated triphenyl phosphate (d15-TPhP), was added to all bulk, hand wipe and air samples prior to analysis and used to adjust all results based on its recovery (range 89.2 −129%) (La Guardia and Hale, 2015). Hand wipe and OVS-2 field

blanks were collected inside each salon near where personal air and hand wipe samples were collected, and analyzed with each sample set. Field blanks were opened, sealed, and transported in a similar manner to personal air and hand wipe samples. A total of five OVS-2 field blanks were collected. TPhP results were below the limit of detection (LOD) for four of the five OVS-2 field blanks, and four of the six hand wipe field blanks. TPHP was also detected in two hand wipe lab processing media blanks. All air and hand wipe samples were adjusted by dividing by the surrogate recovery percentage and subtracting any lab processing media blank or field blank amount. In the event both a media and field blank were above the LOD, the highest blank value was used for correction.

2.7. Statistical Analysis

Descriptive statistics are provided as frequency (%), mean ± standard deviation (SD), median, and range for characteristics of participating nail salon workers. The distributions of the concentrations of TPhP in air and hand wipes, and of DPhP in urine were right-skewed. Therefore, logarithm transformation was applied to the resulting concentrations. A visual determination of the Q-Q plot indicated that the data were lognormal. Air sampling TPhP concentrations from the two consecutive sampling days were averaged using the time-weighted average (TWA) method for each worker, consistent with previous studies reporting similar exposures (Estill et al., 2019; 2020). Two workers had results for only one air concentration due to laboratory sampling error so their single result was used. All hand wipe concentrations were above the limit of detection (LOD) but three air samples had values that were below the LOD. All participants had DPhP urine post-shift concentrations above the LOD, while three participants had non-detectable DPhP urine pre-shift concentrations. The LOD divided by square root of two was substituted for non-detectable TPhP air and DPhP urine pre-shift concentrations (Hornung and Reed, 1990). Additionally, median, geometric mean (GM), geometric standard deviation (GSD), 25^{th} and 75^{th} percentiles, and concentration range were presented for TPhP TWA air, TPhP pre-shift, post-shift, and averaged hand wipe, and DPhP urine pre- and post-shift concentrations.

A Wilcoxon signed-rank test was utilized to examine differences between TPhP hand wipe pre- and post-shift concentrations, and DPhP pre- and post-shift concentrations, while Wilcoxon rank-sum and Kruskal-Wallis tests were utilized to determine concentration differences among pertinent variables, (i.e., paper or cloth medical mask use, glove use, and nail polish). Respective one-sample Student's *t*-test and two-sample Welch's *t*-test were conducted to determine differences of logarithms of urine pre- and post-shift concentrations, and to compare either urine pre-shift or post-shift concentration with the general population and corresponding subpopulations from the NHANES data, in which sampling techniques were utilized to obtain GMs and GSDs. A marginal regression model using generalized estimating equations and incorporating an exchangeable working structure was utilized to account for the statistical correlation among nail technicians from the same salon (Liang and Zeger, 1986). Small-sample corrections were applied to adjust for negatively biased regression parameter standard error estimates (Ford and Westgate, 2017; Westgate, 2016). Analyses were carried out using logarithm of DPhP urine post-shift concentrations as the dependent variable and adjusting for logarithm of DPhP urine pre-shift concentrations. Covariates, including TPhP air and hand wipe post-shift concentrations, sex, age, body mass

index (BMI) in kg/m^2, length of working time in years, glove use (no, intermittent, yes), paper or cloth medical mask use (yes, no), count of regular nail treatments workers polished over two days, acrylic nails service provided (no, yes), last shift worked (yesterday, 2 or more days ago), and worker's nails polished the previous week (no, yes), were evaluated. All statistical tests were two-sided at the 0.05 significance level. 95% confidence intervals (CIs) were provided for univariable and multivariable analyses (Pan and Wall, 2002). Analyses were performed in R version 3.1.2 (R Core Team, 2019).

3. RESULTS

3.1. Demographics

Twelve nail salon workers from four different salons consented to participate in this study (Table's 1 and 2). Most of the subjects were female (83.3%) and all of them were Asian. Median age was 45.6 years (range 35 – 64 years). Most subjects (75%) worked the previous day. A slight majority of the participants (58.3%) did not wear gloves, a paper or cloth medical mask, or nail polish during the previous week. Three out of four salons provided acrylic nails services. The nail technicians worked for an average of nearly 8hours per day (or 15 hours and 42 mins over two days). All nail shops had only general room ventilation and no local exhaust ventilation.

3.2. Bulk Results

Fifteen products were analyzed from the four salons (Table 3). Eleven of the products were regular nail polish, and TPhP was detected in eight of the 11 products. Three polishes likely had intentional TPhP nail polish additive (≥ 1% by weight) and five likely had impurities (< 1% by weight) with ranges of 1.31 – 3.46 and 0.002 – 0.083, respectively. Of the "other products" analyzed in this study, only one sample of top coat detected TPhP (2.46 % by weight). One sample of gel polish was analyzed and TPhP was not detected (Table 3).

3.3. Air and Hand Wipe Results

Personal TWA air samples TPhP were collected from 12 nail salon workers, and every worker had at least one full-shift sample. The GM of TPhP air sampling concentrations was 7.39 ng/m^3 (range 2.94 – 21.85 ng/m^3) (Table 4). Compared to participants who did not wear a paper or cloth medical mask (GM = 5.23 ng/m^3), those wearing masks had significantly higher TPhP air concentrations (GM = 12.01 ng/m^3; p = 0.048).

Hand wipe samples for 11 workers were available for this study (one worker's sample vials broke in transit). The GM of averaged TPhP hand wipe concentrations was 1.07 μg/sample (range 0.17 – 4.36 μg/sample) (Table 4). In addition, post-shift TPhP levels in hand wipe samples were statistically higher (p = 0.024) than pre-shift TPhP hand wipe concentrations (GM = 1.35 and 0.29 μg/sample, respectively). No significant difference in hand wipe TPhP post-shift concentrations was found for those who wore gloves or who recently wore nail polish.

3.4. Urine Results

DPhP was detected in 75% of urine pre-shift samples and 100% of post-shift urine samples. DPhP urine post-shift concentrations (GM = 1.35 μg/g creatinine) were significantly higher than pre-shift concentrations (GM = 0.84 μg/g creatinine; p = 0.012) (Table 5). Urinary concentrations from nail salon workers were compared with the US general population and four subgroups aged 18 years and older including female population, population not born in the US, non-Hispanic Asians, and non-Hispanic Asians not born in the US (Table 5). DPhP urine post-shift concentrations in nail salon workers were significantly higher than concentrations among the general population (p=0.034), the population not born in the US (p = 0.024), non-Hispanic Asians (p = 0.007), and non-Hispanic Asians not born in the US (p = 0.007). The GM of DPhP urine post-shift concentrations was higher than the GM of concentrations among the female population but were not significantly different. Statistically significant differences were observed when comparing post-shift urine concentrations of nail salon workers with the 95% upper CI bounds around GM concentrations from the general population and the other subpopulations (respective p = 0.047, 0.043, 0.016, and 0.019). This comparison shows that the average worker's urinary result in this study was higher than the 95% upper CIs around GMs of these general population groups.

Results of univariable analyses with logarithm of DPhP urine post-shift concentration (adjusted for pre-shift) as the dependent variable are provided in Table 6. For every μg/sample increase in TPhP hand wipe post-shift concentration, DPhP urine post-shift concentrations increased by 3.42 μg/g cr (95% CI: 1.67 – 7.01). Males were more likely to have greater DPhP urine concentration relative to females (1.82 times higher; 95% CI: 1.43 – 2.30), though our sample size for males was small (N=2). Salons providing acrylic nail service had 1.38 times higher DPhP urine post-shift concentrations, compared to those not providing this service (95% CI: 1.06 – 1.82). Additionally, workers who had last worked two or more days ago (GM = 0.43 μg/g cr) had 0.41 times lower DPhP urine pre-shift concentrations relative to those who worked the previous day (GM = 1.05 μg/g cr) (95% CI: 0.21 – 0.78) (Table 6 and Figure 1). The number of days since last shift worked had a trend effect on urine pre-shift concentrations (p < 0.001). In multivariable results, adjusting for logarithm of urine pre-shift concentration, hand wipe post-shift concentrations and sex (females versus males) had significant impacts on the dependent variable, logarithm of urine post-shift concentration (95% CIs: 1.04 – 1.12 and 0.63 – 0.76, respectively) (Table 7).

4. DISCUSSION

This study characterized occupational exposure to TPhP among 12 nail technicians from four nail salons. Nail salon workers are not a transient workforce (e.g., 45% of nail salon workers have been in the field for at least 12 years) (Nails Magazine, 2018), suggesting chronic low-dose TPhP exposure may be a cause for concern for workers in this industry (Kim et al., 2019; Mendelsohn et al., 2016; Young et al., 2018). TPhP concentrations were characterized for bulk, air and hand wipes, and concentrations of DPhP were measured in spot urine samples. About half of the nail technicians did not wear gloves and did not wear respiratory protection. Those who did wear respiratory protection wore a paper or cloth medical mask which is not protective for aerosolized particles or vapors. Though TPhP

likely exists as a gas or vapor, we recommend nail salon technicians consider wearing a NIOSH-approved filtering respirator (e.g., N95) during job tasks that aerosolize particles (e.g., filing and buffing nails).

Fifteen bulk nail polish or coat samples were collected from the four salons, and TPhP was detected in the majority of bulk samples (66.6%). Eleven of the 15 bulk samples were regular nail polish, and they were more likely (82%) to contain TPhP levels above the LOD compared to other nail salon products (gel polish, base coat, etc.; 25% above LOD), though our sample size for other nail salon products was small. Only three of the nail polishes measured contained one percent TPhP or more. Our results are comparable to previous studies reporting TPhP detection levels ranging from 60–100% of nail polishes sampled (Broadwater and Chiu, 2019; Mendelsohn et al., 2016; Young et al., 2018). TPhP concentrations in bulk results from regular polish had a median of 0.083% by weight (range from non-detectable to 3.46%), lower than previously reported medians of 0.89% (Mendelsohn et al., 2016) and 0.273% by weight (Young et al., 2018). However, the maximum concentration of TPhP found in nail polish from our study (3.46% by weight) was higher than reported by Mendelsohn et al (1.68%). These results suggest nail polishes can contain TPhP, potentially exposing nail salon workers during application.

Maximum personal TPhP air concentrations from our study (21.85 ng/m^3) were far below the OEL. The OEL was set to be protective of eye and skin dermatitis and irritation, therefore other chronic outcomes from exposure to TPhP may still be a cause for concern. They were also lower but within the same order of magnitude of air concentrations collected from a nail salon reported in a recent publication (43.7 ng/m^3) (Kim et al., 2019). TPhP air concentrations for all nail salon workers were above the detectable levels, suggesting inhalation may be an important pathway of exposure to TPhP for this industry.

GM hand wipe concentrations for this study were 1.06 μg/sample. Post-shift TPhP hand wipe concentrations (GM 1.35 μg/sample) were significantly higher than pre-shift concentrations (GM 0.29 μg/sample). These results suggest these nail salon workers are dermally exposed to TPhP during their shift. A previous study noted urinary concentrations of DPhP significantly decreased when individuals applying nail polish wore gloves, suggesting dermal may be a primary route of exposure (Mendelsohn et al., 2016), though we found no significant differences.

DPhP was detected in all post-shift urine samples collected in this study and 75% of pre shift-samples, unsurprising considering TPhP has a half-life of 9.5 days (Wang et al., 2020). Post-shift concentrations were significantly higher than pre-shift concentrations for DPhP, similar to TPhP hand wipe results. Similarly, Mendelsohn et al. found a seven-fold increase in DPhP concentrations 10–14 hours after application(Mendelsohn et al., 2016). Another recent study found similar pre-shift (GM 1.1 μg/g) and post-shift (GM 1.3 μg/g) urinary DPhP concentrations across one day of sampling of nail salon technicians (Craig et al., 2019). When comparing DPhP concentrations in nail salon workers to the general population, we found post-shift concentrations were marginally and significantly higher than the GM and its corresponding upper bound of 95% CI, respectively, for the general population. Notably, all of the participants in this study were non-Hispanic Asian. When

we accounted for this fact and compared participants' urinary DPhP concentrations to those collected from the non-Hispanic Asian USA general population, the magnitude of the difference was even larger. When examining differences by type of services offered, we found nail technicians working in salons providing acrylic nails service had significantly higher DPhP urine post-shift concentrations relative to those not providing this service. Interestingly, males in this study were more likely to provide acrylic services than females, which may at least partially explain why males had higher DPhP urine post-shift concentrations. We did not take bulk samples of any acrylic products, and it's possible acrylic products contain TPhP (Environmental Working Group). It is also possible that the acrylic application process creates more particulate concentration from use of powered rotary filing tools to shape acrylic nails (Broadwater and Chiu, 2019). No difference was detected between nail technicians who wore nail polish and those who did not, possibly because their occupational exposures outweighed any increase from personal wearing of the nail polish.

Univariable analysis with DPhP urine post-shift concentrations as the outcome variable were significantly associated with increased TPhP hand wipe post-shift concentrations ($p = 0.028$). We found that technicians who worked more recently had higher baseline (pre-shift) concentrations of DPhP than those who last worked two or three days previously. The pre- and post-shift urinary concentrations suggest nail salon workers are occupationally exposed to TPhP. Additionally, the significant difference in pre-shift/post-shift hand wipe concentrations, and the association between DPhP post-shift concentrations and post-shift hand wipe concentrations (Table 7) suggest the dermal exposure pathway can be relevant for nail salon workers. In addition to inhalation and dermal exposure, transdermal exposure to TPhP is also possible, as one study found semi-volatile organic compound vapors can be directly absorbed into skin through air exposure (Weschler et al., 2015).

This study had some limitations. The sample size for this study (n=12) was relatively low. However, we collected samples over a two-day work period from each participant to better capture accurate information on their occupational exposures. All nail salons in this study were in California, so caution should be exercised when extrapolating results to all nail salon workers in the United States. Urine samples were collected once a day over two days rather than at the beginning and end of each sampling day. The reported half-life of 9.5 days is longer than the time elapsed between shifts over the two sampling days. However, nail salon technicians who worked the day before sampling had higher pre-shift urinary concentrations compared to workers who hadn't worked for at least two days. We also found post-shift urinary concentrations were significantly higher than pre-shift urinary concentrations. These findings suggest that even though TPhP has a relatively long half-life, nail salon technicians' DPhP urinary concentrations decrease when they aren't working while also increasing during the shift. TPhP has other metabolites (e.g., OH-TPhP, MPhP) not included in this study, but DPhP, has been used in previous exposure studies including NHANES (Ospina et al., 2018), allowing us to compare to the general population. DPhP exists on its own and has been found in dust samples (Björnsdotter et al., 2018) and is also a metabolite for the following chemicals: isopropylphenyl diphenyl phosphate, tbutylphenyl diphenyl phosphate, and 2-ethylhexyl diphenyl phosphate (Nishimaki-Mogami et al., 1988; Phillips et al., 2020; Shen et al., 2019). Additionally, TPhP is used in plastics, foams, and

other products (e.g. acrylic products) potentially found in a nail salon. Because of these limitations, it is possible DPhP measured in urine collected from nail salon technicians came from exposures to products other than TPhP in nail polish. More frequent hand wipe and urine sample collection as well as air sampling that differentiates between particle and vapor-phase could have provided us with a more accurate exposure assessment for specific products used by the nail salon technicians. Future studies could examine how acrylic products contribute to nail salon technicians' TPhP exposure. It would also be beneficial if future studies analyzed urine samples for TPhP's other metabolites to gain a fuller picture of nail salon technicians' TPhP exposure. This study only focused on nail salon technicians in California, and a larger study sampling workers from across the country would provide a better understanding of TPhP exposures for this industry. For instance, a larger study could demonstrate the efficacy of wearing butyl gloves to reduce dermal exposure to TPhP, something this study was unable to do. Follow-up studies could also sample for a more comprehensive list of chemicals to which nail salon technicians might be exposed. This study only focused on exposures to TPhP, and other chemicals nail salon workers may be occupationally exposed to like formaldehyde and toluene were not summarized

This study was confined to exposure to TPhP, but other hazards to nail technicians include musculoskeletal hazards and exposure to other chemicals, such as formaldehyde, toluene, ethyl methacrylate. As outlined in OSHA's guide for nail salon workers (OSHA, 2012) efforts should be taken to ensure nail salon workers are provided respiratory protection, fit-tested and taught when to use respiratory protection (e.g., workers conducting filing and buffing create aerosolize particles and should consider N95 respirators). Similarly, butyl gloves are recommended during the application of nail polish and other procedures to reduce potential exposures, though future studies are warranted to further examine this issue.

5. CONCLUSIONS

Results from this study demonstrate nail salon workers may be occupationally exposed to TPhP during application of nail polish. Participants who worked more recently had higher baseline urine concentrations of DPhP, suggesting they could be occupationally exposed to TPhP. Nail salon workers' TPhP hand wipe concentrations rose during the work day, as did their urinary DPhP concentrations. Urinary DPhP concentrations were correlated with post-shift hand wipe TPhP concentrations, suggesting dermal may be a primary exposure pathway. Efforts should be taken to ensure nail salon workers get fit-tested and wear N95 respirators and gloves during job tasks that aerosolize particles.

6. ACKNOWLEDGEMENTS

We would like to thank Chrissy Toennis, Deborah Sammons, Shirley Robertson, and Barb McKenzie for assistance in collecting, processing and submitting urine samples for analysis. We thank Minhthu Le for interpreting at nail salons. We thank Jen Roberts, Fariba Nourian, and Jim Arnold for their assistance with understanding of environmental sample results. We thank Paula Restrepo and Zack Davis for assistance in analyzing the urine samples. Most of all, we thank the workers for participating in the study. This study was approved by the Institutional Review Board at NIOSH. This study was supported in part by an interagency agreement between NIOSH and the National Institute of Environmental Health Sciences (AES15002) as a collaborative National Toxicology Program research activity. The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position of NIOSH, Centers for Disease Control and Prevention. Mention of any

company or product does not constitute endorsement by NIOSH. This paper is Contribution No.3943 of the Virginia Institute of Marine Science, College of William & Mary.

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Highlights:

- Nail salon technicians appear to be occupationally exposed to triphneyl phosphate.
- Post-shift triphenyl phosphate hand wipe concentrations were higher than pre-shift.
- Dermal contact may be a relevant exposure pathway for nail salon technicians.

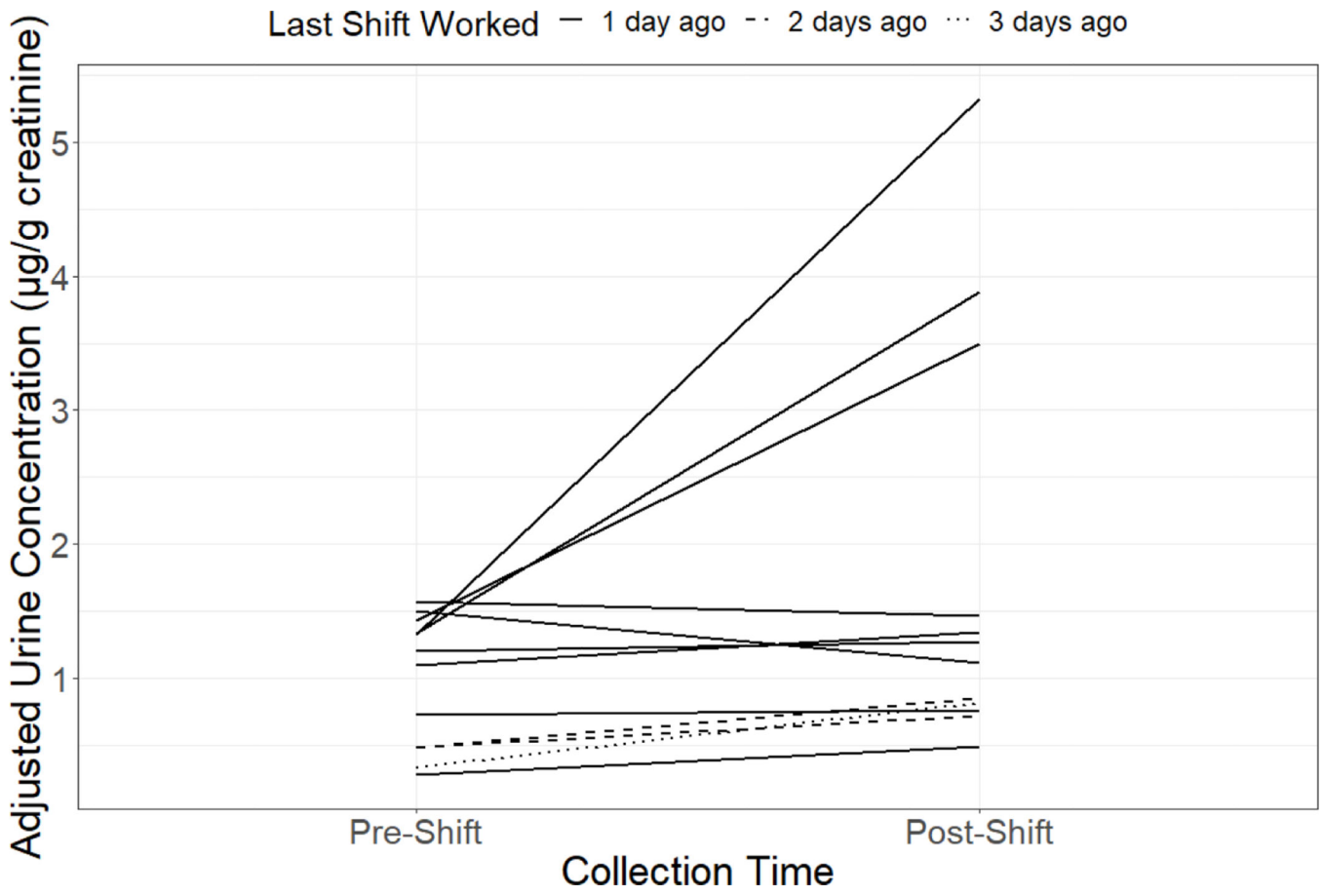

Figure 1.
Adjusted DPhP Urine Concentration (µg/g creatinine) by Collection Time (Pre- and Post-Shift), N=12.

Table 1.

Characteristics of Nail Salon Workers, N=12.

Characteristic	Frequency (%)	Mean (SD)	Median (Range)
Sex			
Male	2 (16.7)		
Female	10 (83.3)		
Race			
Asian	12 (100)		
Ethnicity			
Not Hispanic or Latino	12 (100)		
Last shift worked			
Yesterday	9 (75.0)		
2 or more days ago *	3 (25.0)		
Hands washed during work shift			
Yes	12 (100)		
Gloves worn			
No	7 (58.3)		
Intermittent	2 (16.7)		
Yes	3 (25.0)		
Paper or cloth medical mask worn			
No	7 (58.3)		
Yes	5 (41.7)		
Worker's nails polished during past week			
No	7 (58.3)		
Yes	5 (41.7)		
Acrylic nails service provided			
No	3 (25.0)		
Yes	9 (75.0)		
Age, years		46.3 (7.5)	45.6 (35.0 – 64.0)
Body Mass Index, kg/m^2		23.3 (3.4)	21.9 (20.5 – 31.2)
Length of time working, years		8.0 (4.3)	7.5 (2.0 – 16.0)
Working time over two days, hours		15.7 (2.4)	16.1 (10.1 – 18.3)
Count of regular nail treatments workers polished over two days		10.0 (5.1)	10.5 (0.0 – 20.0)

* Two workers worked two days ago and one worker worked three days ago.

Table 2.

Nail Salons Recruited in the San Francisco Area in California, USA, in 2016.

Facility Site	Salon Size (ft^2)	Operating Hours (per day)	Acrylic Nails Service Provided	Last Shift Worked	Gloves Worn	Paper or Cloth Medical Mask Worn	Working Hours Over Two Days	Regular Nail Polish Applied Over Two Days (Number of Sets)
Salon A	580	9	No					
				Yesterday	Intermittent	No	17.4	12
				Yesterday	No	No	18.2	15
				2 days ago	Yes	Yes	10.1	11
Salon B	608	8	Yes					
				Yesterday	No	Yes	15.9	1
				2 days ago	No	Yes	13.3	10
				Yesterday	No	Yes	16.2	12
Salon C	300	9	Yes					
				3 days ago	No	No	18.4	8
				Yesterday	No	No	15.7	6
				Yesterday	No	No	17.3	9
Salon D	540	8	Yes					
				Yesterday	Yes	No	16.2	20
				Yesterday	Yes	No	16.1	6
				Yesterday	Intermittent	Yes	13.5	12

Table 3.

TPhP Levels in Nail Salon Polishes and Other Products.

Product	Brand	Product Name, Type (Brand Location)	TPhP (% by Weight) *
Regular Polish (N=11)	OPI	Infinite Shine 2, lacquer (North Hollywood, CA)	ND
	OPI	Nail Lacquer, lacquer (North Hollywood, CA)	2.08
	Zoya	Professional Lacquer, lacquer (Cleveland, OH)	0.014
	Savina	Nail Lacquer, lacquer (Unknown)	0.002
	Alvia	Nail Lacquer, lacquer (Norcross, GA)	1.31
	Sation	Nail Lacquer, lacquer (Unknown)	0.008
	Alvia	Nail Lacquer, lacquer (Norcross, GA)	3.46
	OPI	Infinite Shine 2, lacquer (North Hollywood, CA)	0.003
	LeChat	Dare To Wear, lacquer (Hercules, CA)	0.083
	Verity	Nail Lacquer, lacquer (Santa Fe Springs, CA)	ND
	Essie	Nail Lacquer, lacquer (Clichy, France)	2.98
Of the 11 regular polishes, 9 were greater than LOD; GM = 0.108 (GSD = 21.66); Median = 0.083			
Other Products (N=4)	OPI	Gelcolor, soak-off gel polish or lacquer (North Hollywood, CA)	ND
	Gena	Healthy Hoof, hoof lacquer (Los Angeles, CA)	ND
	Zoya	Armor, top coat (Cleveland, OH)	2.46
	ORLY	Bonder, rubberized base coat (Los Angeles, CA)	ND

* ND: non-detected. Samples were categorizedd as ND when TPHP levels were lower than the detection limit of 0.10 μg/g.

Table 4.

TPhP Air (ng/m^3) and Hand Wipe (μg/sample) Concentrations.

Environmental	**N**	**Median**	**GM (GSD)**	**25th, 75th %tiles**	**Range**	**P-value**
TWA Air †	12	7.16	7.39 (2.06)	3.91 – 13.85	2.94 – 21.85	
Hand Wipe Average	11	1.43	1.07 (3.25)	0.31 – 3.24	0.16 – 4.36	
Hand Wipe Pre	11	0.22	0.29 (4.90)	0.07 – 1.16	0.02 – 3.18	0.024
Hand Wipe Post	11	1.26	1.35 (4.00)	0.32 – 5.30	0.22 – 7.91	
Paper or cloth medical mask Worn *	**N**	**Median Air**	**GM (GSD)**	**25th, 75th %tiles**	**Range**	**P-value**
No	7	4.00	5.23 (1.85)	3.11 – 8.76	2.94 – 15.77	0.048
Yes	5	11.94	12.01 (1.83)	10.89 – 18.78	4.69 – 21.85	
Glove Worn ‡	**N**	**Median Hand Wipe Post**	**GM (GSD)**	**25th, 75th %tiles**	**Range**	**P-value**
No	6	0.61	0.91 (4.69)	0.26 – 5.30	0.22 – 6.82	0.322
Intermittent	2	0.83	0.72 (2.24)	0.40 – 1.26	0.40 – 1.26	
Yes	3	4.09	4.52 (1.68)	2.84 – 7.91	2.84 – 7.91	
Worker's nails polished during past week ‡	**N**	**Median Hand Wipe Post**	**GM (GSD)**	**25th, 75th %tiles**	**Range**	**P-value**
No	7	0.90	1.07 (4.37)	0.26 – 5.30	0.22 – 6.82	0.412
Yes	4	2.68	2.02 (3.71)	0.83 – 6.00	0.40 – 7.91	

*Results using TWA air concentrations.

†Air sampling time, hours per day, with mean ± standard deviation = 7.8 ± 1.2, median = 8.1, and range = 5.0 – 9.1.

‡Results using post-shift hand wipe concentrations.

Table 5.

Analyte DPhP Urine Sampling Results.

	N (N<LOD*)	GM (GSD)	Median	Range	Difference of Post and Pre GMs	P-value # (Post GM vs. Pre GM)
Adjusted Pre-Shift (μg/g-creatinine)	12 (3)	0.84 (1.88)	1.15	0.27 – 1.57	0.51	0.012
Adjusted Post-Shift (μg/g-creatinine)	12 (0)	1.35 (2.12)	1.19	0.49 – 5.33		
Unadjusted Pre-Shift (μg/L)	12 (3)	0.57 (3.07)	0.69	0.11 – 2.39	0.68	0.027
Unadjusted Post-Shift (μg/L)	12 (0)	1.25 (2.64)	1.27	0.29 – 6.32		

	N (N<LOD *)	GM (GSD) (μg/g-cr)	Difference of Pre and Pop. GMs	P-value † (Pre GM vs. Pop. GM)	Difference of Post and Pop. GMs	P-value † (Post GM vs. Pop. GM)
General Population (Pop.) ‡	1901 (187)	0.80 (2.59)	0.04	0.797	0.55	0.034
Female Population ‡	980 (102)	1.03 (2.73)	−0.19	0.298	0.32	0.239
Population Not Born in the USA ‡	539 (74)	0.76 (2.62)	0.08	0.609	0.59	0.024
Non-Hispanic Asians ‡	229 (48)	0.65 (2.54)	0.19	0.208	0.70	0.007
Population Not Born in the USA and Non-Hispanic Asians ‡	195 (44)	0.65 (2.54)	0.19	0.221	0.70	0.007

	N (N<LOD *)	95% Upper CI	Difference of Pre GM and 95% Upper CI	P-value § (Pre GM vs. 95% Upper CI)	Difference of Post GM and 95% Upper CI	P-value § (Post GM vs. 95% Upper CI)
General Population (Pop.) ‡	1901 (187)	0.83	0.01	0.976	0.52	0.047
Female Population ‡	980 (102)	1.10	−0.26	0.168	0.25	0.353
Population Not Born in the USA ‡	539 (74)	0.82	0.02	0.928	0.53	0.043
Non-Hispanic Asians ‡	229 (48)	0.73	0.11	0.480	0.62	0.016
Population Not Born in the USA and Non-Hispanic Asians ‡	195 (44)	0.75	0.09	0.535	0.60	0.019

*Limit of detection (LOD) for DPhP is 0.16 in μg/L.

#A one-sample Student's *t*-test was utilized to examine differences of logarithm urine pre- and post-shift concentrations.

†A two-sample Welch's *t*-test, accounting for heterogeneous variances, was utilized to compare adjusted pre-shift or post-shift urine data (μg/g creatinine) with the general population and four subpopulations.

§A one-sample Student's *t*-test was utilized to compare adjusted pre-shift or post-shift urine GMs (μg/g creatinine) with the 95% upper confidence intervals around GMs from the general population and four subpopulations.

‡Ospina M, Jayatilaka N, Wong L, Restrepo P, Calafat AM. (2018) Exposure to organophosphate flame retardant chemicals in the U.S. general population: Data from the 2013–2014 National Health and Nutrition Examination Survey. *Environment International*; 110: 32–41. Includes

participants aged 18+. In order to obtain GMs and GSDs for general population and four subpopulations, sample weights, as well as variables that identify the sample strata and specify primary sampling unit, were account for the analyses.

Table 6.

Univariable Analysis, Using Logarithm of Urine Concentration (μg/g creatinine) as the Outcome of Interest, N=12.

	Estimate (SE)	Factor *	95% CI #	P-value #
Dependent variable: Logarithm (Urine Post-Shift, μg/g creatinine) Adjusted independent variable: Logarithm (Urine Pre-Shift, μg/g creatinine)				
TWA air, ng/m^3	−0.005 (0.018)	0.995	0.956, 1.035	0.790
Hand wipe post-shift, μg/sample	1.231 (0.292)	3.424	1.673, 7.005	0.006
Sex				
Female	Ref †	Ref †		
Male	0.598 (0.088)	1.818	1.433,2.304	0.002
Age, years	0.004 (0.018)	1.004	0.962, 1.049	0.822
BMI, kg/m^2	−0.004 (0.023)	0.996	0.945, 1.050	0.879
Length of working time, years	−0.001 (0.008)	0.999	0.968, 1.030	0.871
Glove worn				
No	Ref †	Ref †		
Intermittent	−0.226 (0.202)	0.798	0.507, 1.256	0.292
Yes	−0.102 (0.207)	0.903	0.524, 1.558	0.647
Paper or cloth medical mask worn				
No	Ref †	Ref †		
Yes	0.078 (0.244)	1.082	0.575, 2.033	0.761
Count of regular nails polished over two days	0.022 (0.034)	1.022	0.955, 1.095	0.519
Acrylic nails service provided				
No	Ref †	Ref †		
Yes	0.325 (0.119)	1.384	1.055, 1.816	0.024
Dependent variable: Logarithm (Urine Pre-Shift, μg/g creatinine)				
Last shift worked				
Yesterday	Ref †	Ref †		
2 or more days ago ‡	−0.904 (0.266)	0.405	0.211, 0.776	0.014
nail polish worn during last week				
No	Ref †	Ref †		
Yes	−0.032 (0.419)	0.969	0.366, 2.561	0.941

* Ref indicates reference group for comparison.

\# A *t*-test with an adjusted degree of freedom (Pan and Wall, 2002) was used to obtain 95% CI and p-value.

† Factor represents exp(estimate).

‡ Two workers worked two days ago and one worker worked three days ago.

Table 7.

Multivariable Analysis, Using Logarithm of Urine Concentration (μg/g creatinine) as the Outcome, N=12.

Model	Estimate (SE)	Factor *	95% CI #	P-value #
Dependent variable: Logarithm (Urine Post-Shift, μg/g creatinine) Adjusted independent variable: Logarithm (Urine Pre-Shift, μg/g creatinine)				
Hand wipe post-shift, μg/sample	0.078 (0.016)	1.081	1.039, 1.124	0.004
Sex				
Female	Ref †	Ref †		
Male	0.368 (0.048)	1.445	1.312,1.590	<0.001

*Factor represents exp (estimate).

#A *t*-test with an adjusted degree of freedom (Pan and Wall, 2002) was used to obtain 95% CI and p-value.

†Ref indicates reference group for comparison.