PHTHALATE DIESTER LEVELS IN PERSONAL AIR SAMPLES DURING PREGNANCY IN TWO URBAN POPULATIONS

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ABSTRACT

There is growing concern over the widespread exposures to phthalates detected in the U.S. population. Phthalates have been shown to be hepatic, reproductive and developmental toxicants. Certain phthalates are elevated in women of reproductive age, resulting in implications for the health of the developing fetus. In the current study, we assess the presence of phthalates in personal air samples of pregnant women subjects in prospective cohorts in Northern Manhattan and Krakow, Poland. Phthalates were detected in 100% of samples. Diethyl phthalate (DEP) (range 1,447-7,123 ng/m^3) and dibutyl phthalate (DBP) (range 755-14,763 ng/m^3) were present at the highest levels in Northern Manhattan and Krakow respectively. Dicyclohexyl phthalate (DCHP), butylbenzyl phthalate (BBzP), diethylhexyl phthalate (DEHP), and disobutyl phthalate (DIBP) were present in ascending order. Demographic characteristics of study subjects are presented to identify possible risk factors. Comparison data are presented for 4 phthalate isomers to assess the significance of these levels.

INDEX TERMS

Phthalate esters, *in utero* exposures, personal air monitoring, DBP, DEP

INTRODUCTION

Exposure to phthalates is common and widespread in the United States. This has been demonstrated in a recent survey published by the Centers for Disease Control in which they report data on urinary phthalate metabolites measured in 1,029 volunteers in 12 locations in the U.S. (CDC, 2001, Blount *et al.,* 2000). The elevated levels of DBP among women of childbearing age is the most alarming from a public health perspective. The current study confirms this finding in two urban populations of pregnant women.

Phthalates induce direct and indirect toxicity to endocrine tissue. DBP acts as an anti-androgen in a non-receptor mediated mechanism, altering the response to endogenous hormones during development (Foster *et al*., 2000). Exposure to DBP during days 12-14 and days 15-17 of pregnancy in the rat resulted in incidence of undescended testes in the male fetuses (Ema *et al.* 2000). DBP exposure is related to reduced sperm counts, decreased fertility and reproductive tract malformation in male offspring (Foster *et al.* 2000). DEHP alters the morphology and functioning of the ovaries resulting in suppression of estradiol and ovulation (Davis *et al.,* 1994). In the human gut, phthalates are metabolized to monoesters that are more toxic than the diester and are responsible for the developmental and reproductive toxicity (Davis *et al.,* 1994).

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Because of the chemical properties they confer, phthalates are used in PVC plastics, cosmetics, construction materials, food packaging, car-care products, medical devices, insecticides and other products. Phthalates in hair products, soaps, lotions, and perfumes may be a significant source of exposure for women of childbearing age. Unlike organochlorines, phthalates have a short half-life in the body (~24 hours-5 days); yet they are consistently present, independent of the time of sampling. Ingestion of contaminated food is the primary source of exposure and inhalation is the second most important pathway (CERHR, 2000).

The current study was initiated to determine whether phthalates are present in the Columbia Center for Children's Environmental Health (CCCEH) study populations of pregnant women in Northern Manhattan and Krakow, Poland. The second question is whether these levels are high enough to warrant a more extensive investigation of external exposures, internal dose, and possible health outcomes. 30 PUF cartridges were selected *a posteriori* from 2 batches of personal air monitoring samples collected from New York and Krakow subjects in 2000-2001 and analyzed for 6 phthalate isomers.

METHODS

Enrollment. Women ages 18-35 were enrolled during pregnancy in the CCCEH study at prenatal clinics in Northern Manhattan (NY), the South Bronx, and Krakow, Poland. In New York, the study was restricted to women who self-identified as African American or Dominican and had resided in Northern Manhattan or the South Bronx for ≥ one year prior to pregnancy. In Krakow, the study was restricted to women who had resided in the city for at least one year and within a 0.5 km radius of two ambient air monitoring stations with the highest and lowest pollution levels. To control for known risk factors of adverse birth outcomes, women were excluded if they smoked cigarettes or used other tobacco products during pregnancy, used illicit drugs, had diabetes, hypertension or known HIV or had had their first prenatal visit after the 20th week of pregnancy. The study was approved by the Institutional Review Boards of Columbia University and Jagellionian University in Krakow and informed consent was obtained from all study subjects.

Questionnaire data. A questionnaire was administered to each woman in her home during the pregnancy that included information on demographics, home characteristics, lifetime residential history, history of active and passive smoking, occupational history, alcohol and drug use during pregnancy and history of residential pesticide use. Because phthalates were not included in the original hypotheses, the questionnaire is not designed to estimate exposures to phthalate-containing products, phthalates in food, or in the ambient environment.

Personal ambient air monitoring. During the 3rd trimester of pregnancy for the NY women and the 2nd trimester for the Krakow women, subjects were asked to wear a small backpack holding a personal ambient air monitor during the daytime hours for two consecutive days and to place the monitor near the bed at night. The backpack was designed so that the sampling inlet was positioned in her breathing zone. The NY personal air sampling pumps operated continuously at 4 liters per minute (LPM) over this period, collecting particles of $\leq$2.5 microns in diameter on a precleaned quartz microfiber filter and semivolatile vapors and aerosols on a polyurethane foam (PUF) cartridge back-up. The same pumps in Krakow were operated at 2 LPM. In the New York samples, an average of 10.7 m^3 of air was drawn through the sampler and in the Krakow samples, an average of 5.1 m^3 was drawn. The personal air monitoring samplers from all women in the cohort are being analyzed for polycyclic aromatic hydrocarbons and results are published elsewhere (Kinney *et al*., submitted). In New York,

the women were monitored between March-July, 2000. In Krakow, they were monitored between November 2000-March 2001.

Phthalates in air monitoring samples. The air monitoring samples were brought to the laboratories at the Mailman School of Public Health and the Jagellionian University, inventoried and frozen. Once per month, air-monitoring samples were shipped on dry ice to Southwest Research Institute and stored at -12^0 C. The PUF and filter were soxhlet extracted with 6% diethyl ether in hexanes, and the extract concentrated to 1.0 mL. GC/MS analysis for the six phthalates was performed using an Agilent 6890 gas chromatograph with a DB-5.625 30m x 25mm i.d. column and an Agilent 5973 Mass Selective Detector in selected ion monitoring mode. The phthalates were quantified by the internal standard method using deuterated PAH as the internal standards. Multiple dilutions were usually needed to bring all analytes within the linear calibration range.

In the New York and Polish samples, 6 phthalate isomers were quantitated: DEHP, BBzP, DBP, DEP, DIBP and DCHP. Results were reported in nanogram amounts for samples, PUF blanks and solvents. An average PUF and solvent blank value was calculated for each isomer separately and then subtracted from the sample value. This amount was divided by the total volume of air drawn for each sample to give the concentration in nanograms per cubic meter. If the blank subtraction resulted in a negative value, then that data point was set to one-half of the blank value. This only occurred with BBzP measurements in 6 samples from Krakow and can be explained by the lower pump volume (2LPM vs. 4 LPM).

Statistical analyses. Descriptive statistics for phthalate concentrations and demographic characteristics were calculated separately for the Northern Manhattan and Krakow subjects using SPSS for Windows 10.1. Data was log transformed before concentration means were compared using independent two-sample *t* tests. Statistically significant differences have a *p-value* of less than .05. DCHP was barely detectable and therefore excluded from the bar graph. Demographic characteristics were summarized using data from the questionnaires. Pearson's correlation coefficients were calculated using the log-transformed data to assess the co-occurrence of phthalate isomers. Four of the isomers are compared to reference data on indoor air concentrations to help determine the significance of the observed levels in these two populations.

RESULTS

All 6 phthalates were detected in 100% of the samples. Results are presented in Table 1.

Table 1. Descriptive Statistics for Phthalate Diesters in 48hr Personal Air Samples in two Urban Populations of Pregnant Women

Conc.	Krakow, Poland (n=30)					Northern Manhattan (n=30)				
(ng/m^3)	Mean	Median	SD	Min	Max	Mean	Median	SD	Min	Max
DEHP	432	368	243	82.8	1,100	227	229	98.9	55.5	430
BBzP	35.1	18.0	44.4	2.74	194	86.7	32.1	148	.10	626
DBP	2,900	2,300	2,500	755	14,800	568	389	733	96.1	4,100
DEP	1,000	843	667	261	2,900	3,000	2,700	1,300	1,400	7,100
DIBP	1,000	808	1,400	307	8,100	417	372	268	31.6	1,300
DCHP	4.09	2.34	9.60	2.23	54.9	2.04	1.92	.90	.12	3.89

The mean concentrations of all of the isomers differ significantly (p<.001) between the New York and Krakow populations except for BBzP (p=.35). The unequal distribution of the phthalate isomers between the two cities can be seen in Figure 1. DEP and DBP are the 2 most prevalent in both settings, even though their relative proportions are reversed.

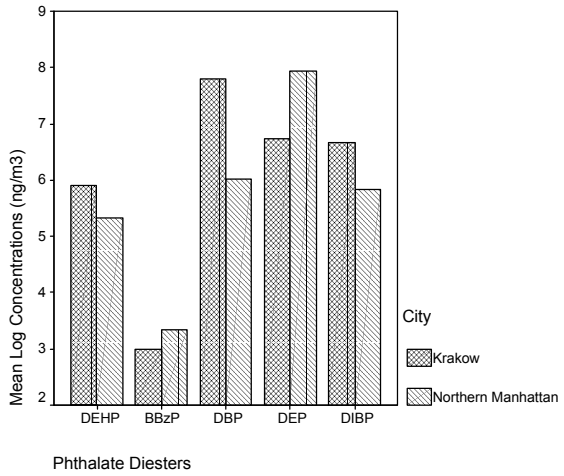

Figure 1. Phthalate Isomer Distribution

In a combined analysis of Northern Manhattan and Krakow data, DBP and DIBP are the most highly correlated (r=.65, p<.001). Other phthalate isomers are mildly correlated such as DBP and DEHP (r=.47, p<.001); DEHP and DCHP (r=.33, p=.01); DBP and DCHP (r=.38, p=.003). Other isomers are negatively correlated such as DBP and DEP (r=.-59, p<.001) and DEHP and DEP (r=-.35 and p=.006).

Demographic characteristics of both populations are reported in Table 2. New York subjects are younger by an average of 5 years and Krakow subjects have an average of 4 more years of education. The New York sample was 70% Dominican or Dominican/American, and 30% African American.

Table 2. Demographic characteristics of study subjects

Characteristic	N		Mean		SD		Range	
	NY	KRA	NY	KRA	NY	KRA	NY	KRA
Age (yrs)[1]	30	30	22	27	3.5	4.1	18-31	18-34
Education (yrs.)	29	30	11	15	2.6	2.7	3-16	11-21
Ethnicity			Northern Manhattan				Krakow	
African American			9 (30%)				0	
Dominican/Dominican American			21 (70%)				0	
Polish			0				30 (100%)	
Income-level[2]								
Low			11 (41%)				19(63%)	
Middle			12 (44%)				3 (10%)	

[1] age at the end of the 48-hr monitoring

[2] In Northern Manhattan, the variable is defined as: low = $0-10,000, middle = $10,000-$30,000, 15% of the subjects had an income between $30,000-80,000. In Krakow, the variable is defined as low = lowest tax bracket and middle = medium tax bracket. 10% of subjects thought the question was inappropriate and 17% did not know the answer.

Table 3 reports the ranges for four phthalate isomers that have been measured in indoor air and reported in the literature. The estimate for BBzP reflects median air levels in 125 California homes. The outdoor levels of the same homes were below detection. The range for DBP reflects the indoor air of a "sick building." The DEP estimates reflect indoor air in a telephone switching facility in Newark, NJ taken over a 43-day period.

Table 3. Comparison data for phthalate diesters in indoor air

Phthalate Diester (ng/m^3)	**Min**	**Max**	Reference
DEHP	**10**	**100**	CERHR-NTP, 2000
BBzP	**0.034-0.035 (median)**		IPCS, 1997
DBP	**1200**	**5900**	Weschler *et al.*, 1990
DEP	**1600**	**2030**	Shields and Weschler, 1987

DISCUSSION AND IMPLICATIONS

In cosmetics, phthalates are used to increase penetration of the skin, as moisturizers and to prevent brittleness in nail polish *(*Houlihan, 2001). Inhalation exposures are largely due to the volatilization of phthalates from cosmetics, home-care products and the off-gassing of construction materials (CERHR, 2000). Large quantities of phthalates are released into the environment during their production and may also be contributing to levels in urban ambient and indoor air (ATSDR, 1999).

Increased exposures to DBP, as measured in urinary metabolites, have been associated with having 12 years or less of education. Elevated BBzP exposures have been associated with a family income of $1,500/month or less at the time of sampling (Koo, 2001). Our sample size was not large enough to test relationships between demographic variables and phthalate exposures.

The disparity in the distribution of the phthalate isomers is most likely due to different types of sources present in the indoor and ambient environments in New York and Poland. Closer investigation into product use in the indoor environment and outdoor air levels is required to clarify this.The co-occurrence of phthalate isomers could be due to the types of products in the woman's environment or their combined use in certain products. This also requires further investigation into the products used among study subjects and the chemical formulations of those products. Phthalate mixtures are often used in the production of PVC plastics, which could partly explain this.

The maximum concentration of DBP measured in Krakow is 2.5-fold higher than the highest measurement in the sick building study. For DEP, the Krakow data falls roughly into the reported range, while the Northern Manhattan exposures are 3.5-fold higher than the maximum measurement. The highest level of DEHP measured in Krakow is higher than the maximum estimate by an order of magnitude. The median levels of BBzP measured in our subjects are nearly 3 orders of magnitude higher than the medians measured in the California homes.

These findings confirm the CDC conclusion that the lower molecular weight phthalates are ubiquitous in the ambient environment and at levels higher than previously assumed. There is

a need for further investigation to better characterize exposures, pathways, and potential risks to the mother and the developing fetus.

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