Urinary Levels of Seven Phthalate Metabolites in the U.S. Population from the National Health and Nutrition Examination Survey (NHANES) 1999–2000

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We measured the urinary monoester metabolites of seven commonly used phthalates in approximately 2,540 samples collected from participants of the National Health and Nutrition Examination Survey (NHANES), 1999–2000, who were ≥ 6 years of age. We found detectable levels of metabolites monoethyl phthalate (MEP), monobutyl phthalate (MBP), monobenzyl phthalate (MBzP), and mono-(2-ethylhexyl) phthalate (MEHP) in > 75% of the samples, suggesting widespread exposure in the United States to diethyl phthalate, dibutyl phthalate or diisobutylphthalate, benzylbutyl phthalate, and di-(2-ethylhexyl) phthalate, respectively. We infrequently detected monoisononyl phthalate, mono-cyclohexyl phthalate, and mono-n-octyl phthalate, suggesting that human exposures to di-isonynyl phthalate, dioctylphthalate, and dicyclohexyl phthalate, respectively, are lower than those listed above, or the pathways, routes of exposure, or pharmacokinetic factors such as absorption, distribution, metabolism, and elimination are different. Non-Hispanic blacks had significantly higher concentrations of MEP than did Mexican Americans and non-Hispanic whites. Compared with adolescents and adults, children had significantly higher levels of MBP, MBzP, and MEHP but had significantly lower concentrations of MEP. Females had significantly higher concentrations of MEP and MBzP than did males, but similar MEHP levels. Of particular interest, females of all ages had significantly higher concentrations of the reproductive toxicant MBP than did males of all ages; however, women of reproductive age (i.e., 20–39 years of age) had concentrations similar to adolescent girls and women ≥ 40 years of age. These population data on exposure to phthalates will serve an important role in public health by helping to set research priorities and by establishing a nationally representative baseline of exposure with which population levels can be compared. *Key words:* mono-(2-ethylhexyl) phthalate, monobenzyl phthalate, monobutyl phthalate, monoethyl phthalate, NHANES, phthalate exposure. *Environ Health Perspect* 112:331–338 (2004). doi:10.1289/ehp.6723 available via *http://dx.doi.org/* [Online 1 December 2003]

Phthalates (dialkyl or alkyl/aryl esters of 1,2-benzenedicarboxylic acid) are a class of widely used industrial compounds [Agency for Toxic Substances and Disease Registry (ATSDR) 1995, 1997, 2001, 2002; David et al. 2001]. Many phthalates have various toxicologic and chemical characteristics and have a spectrum of industrial applications. Phthalates have numerous uses as softeners of plastics, solvents in perfumes, and additives to hairsprays, lubricants, and insect repellents (ATSDR 1995, 1997, 2001, 2002; David et al. 2001). In the residential construction or automotive industries, di-(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), and benzylbutyl phthalate (BzBP) are used in floorings, paints, carpet backings, adhesives, wood finishers, wallpaper, and in polyvinyl chloride (PVC) products (ATSDR 2002, 2001). Although phthalates have low volatility, they off-gas and are present in residential indoor air (Rudel et al. 2003). DEHP has been found in the air inside cars at levels from 1 to 34 $\mu g/m^3$; indoor residential measurements of DEHP that were taken in the spring of 2000 ranged from 0.04 to 0.23 $\mu g/m^3$ (ATSDR 2002). People are at risk of exposure because the phthalates can be absorbed through the skin, inhaled, ingested, or directly administered to patients through transfusions or other medical procedures that use PVC or vinyl medical devices (ATSDR 1995, 1997, 2001, 2002). After human exposure, phthalates are rapidly metabolized to their respective monoesters. These monoesters are then further metabolized by oxidation and/or glucuronidation to increase their water solubility, which facilitates their urinary excretion (ATSDR 1995, 1997, 2001, 2002; Silva et al. 2003a).

Phthalates are a concern in environmental public health because of the high potential for human exposure to phthalates and their demonstrated toxicity in animals. DEHP is a rodent carcinogen (ATSDR 2002; Huber et al. 1996). DEHP, DBP, BzBP, and several phthalate metabolites, such as monobutyl phthalate (MBP), monobenzyl phthalate (MBzP), and mono-(2-ethylhexyl) phthalate (MEHP), are teratogenic in animals (Ema and Miyawaki 2001a, 2001b; Foster et al. 2001; Gray and Gangolli 1986; Mylchreest et al. 1998; Parks et al. 2000). Human studies are scarce, but monoethyl phthalate (MEP) has shown an association with sperm DNA damage (Duty et al. 2003).

Understanding human exposure to phthalates requires information on the concentration of these toxicants in the general population and on the pharmacokinetics of the phthalates. Because of the ubiquity of the parent phthalate diesters, human studies using these as biomarkers have involved highly exposed populations (Ching et al. 1981; Dirven et al. 1993; Faouzi et al. 1999; Mettang et al. 1996; Pollack et al. 1985). Therefore, we used phthalate monoester metabolites as markers (Blount et al. 2000a; Silva et al. 2003b) to assess phthalate exposure to the general population [Blount et al. 2000b; Brock et al. 2002; Centers for Disease Control and Prevention (CDC) 2001, 2003; Hoppin et al. 2002].

We report nationally representative concentrations in the United States of MEP, MBP, MBzP, and MEHP in individuals ≥ 6 years of age, stratified by age group, sex, and race/ethnicity.

Materials and Methods

Survey design. The National Health and Nutrition Examination Survey (NHANES), conducted by the National Center for Health Statistics (NCHS) of the CDC, is an ongoing survey designed to measure the health and nutrition status of the civilian noninstitutionalized U.S. population ≥ 2 months of age (NCHS 2003). National population estimates for phthalate metabolites can be derived from each 2-year cycle of the survey.

The sampling scheme for the NHANES 1999–2000 cycle is a complex multistage area probability design. Adolescents 12–19 years of age, adults ≥ 60 years of age, low-income people, non-Hispanic blacks, and Mexican Americans were oversampled (i.e., sampled at a higher proportion than were subjects in other demographic groups). Data were collected by household interviews and by standardized physical examinations conducted in mobile examination centers. Participation of the human subjects involved in this research occurred only

after informed consent was obtained. Urine specimens for analyses, including phthalate metabolites and creatinine concentrations, were collected from each participant ≥ 6 years of age during one of three daily examination periods (0830–1200 hr, 1230–1600 hr, 1630–2000 hr). Sociodemographic information and medical histories of the survey participants and their families were collected during the household interviews (NCHS 2003).

NHANES 1999–2000 was conducted in 26 locations throughout the United States and included examinations of 9,282 people. For phthalate monoester measurements, we analyzed a random one-third subset of samples. Because the subset was a random selection of samples from the entire set, the representational aspect of the survey was maintained (NCHS 2003).

Laboratory methods. After collection, the urine specimens were aliquoted and then

Table 1. GM and selected percentiles of MEP concentrations in urine [in µg/L and µg/g creatinine (95% CI)] for the U.S. population ≥ 6 years of age from NHANES 1999–2000.

| | GM | Selected percentiles | | | | | | No. |
		10th	25th	50th	75th	90th	95th	
Total	179 (159–201)	28.9 (23.6–34.2)	61.4 (54.0–69.7)	164 (142–192)	450 (378–523)	1,260 (988–1,490)	2,840 (2,020–4,070)	2,536
	163 (148–179)[a]	*33.0 (29.1–35.8)*	*64.7 (57.5–73.5)*	*141 (132–155)*	*360 (313–411)*	*898 (762–1,150)*	*1,950 (1,460–2,730)*	
Age group (years)								
6–11	91.3 (73.0–114)	27.2 (20.4–35.7)	40.8 (35.9–46.8)	74.7 (50.6–107)	197 (129–259)	378 (290–644)	756 (379–1,070)	328
	92.6 (74.2–116)	*29.7 (24.9–34.9)*	*45.6 (33.6–57.7)*	*79.4 (61.2–121)*	*165 (124–208)*	*341 (219–559)*	*625 (365–784)*	
12–19	211 (167–266)	32.7 (22.4–50.6)	72.4 (53.6–99.8)	193 (141–256)	558 (432–806)	1,510 (1,060–2,100)	3,260 (1,670–4,100)	752
	142 (120–168)	*29.8 (27.0–33.5)*	*50.7 (41.4–57.9)*	*122 (86.2–168)*	*361 (279–495)*	*879 (676–1,260)*	*1,550 (907–2,030)*	
≥ 20	190 (168–214)	27.7 (22.0–34.5)	63.3 (56.7–74.9)	180 (154–210)	482 (409–555)	1,340 (1,010–1,660)	3,480 (2,210–5,100)	1,456
	179 (161–199)	*34.5 (29.1–39.1)*	*75.6 (66.3–83.6)*	*154 (139–170)*	*390 (338–452)*	*1,010 (810–1,440)*	*2,170 (1,670–3,490)*	
20–39	224 (184–272)	31.8 (22.7–47.5)	78.6 (61.4–93.2)	211 (164–263)	526 (434–719)	1,442 (986–2,453)	3,872 (1,893–9,463)	532
	178 (147–216)	*33.6 (24.6–40.3)*	*74.9 (58.6–90.6)*	*154 (132–184)*	*376 (300–484)*	*1,149 (673–1,865)*	*2,661 (1,442–4,071)*	
≥ 40	161 (148–186)	26.8 (19.2–31.3)	58.7 (48.0–65.1)	152 (129–180)	410 (342–518)	1,125 (892–1,491)	2,746 (1,678–4,560)	924
	180 (163–199)	*34.8 (28.5–42.3)*	*76.1 (64.9–84.2)*	*150 (136–172)*	*404 (336–476)*	*996 (803–1,342)*	*2,064 (1,462–3,348)*	
Sex								
Males	179 (157–204)	28.4 (23.8–35.4)	54.7 (48.3–64.1)	154 (121–191)	523 (400–621)	1,430 (1,150–2,090)	3,480 (2,270–4,330)	1,214
	141 (124–159)	*27.6 (22.6–33.1)*	*48.9 (40.3–60.8)*	*120 (106–138)*	*324 (268–391)*	*996 (761–1,420)*	*1,940 (1,460–2,900)*	
Females	178 (154–206)	28.0 (21.8–32.1)	65.0 (57.6–80.2)	174 (145–205)	425 (356–482)	977 (825–1,340)	2,230 (1,330–4,100)	1,214
	187 (167–209)	*42.7 (34.7–51.7)*	*81.4 (73.4–94.8)*	*157 (142–182)*	*377 (333–453)*	*821 (719–1,150)*	*1,920 (1,100–3,410)*	
Race/ethnicity								
MA	181 (163–201)	30.2 (25.2–38.1)	66.8 (56.6–77.4)	174 (150–205)	441 (410–510)	1,250 (893–1,410)	1,720 (1,410–2,450)	813
	164 (145–186)	*36.3 (29.2–41.5)*	*63.4 (53.6–77.9)*	*154 (136–175)*	*382 (323–469)*	*814 (692–886)*	*1,330 (1,010–1,860)*	
NHW	322 (278–373)	56.1 (48.3–73.2)	127 (111–143)	306 (256–350)	789 (588–996)	1,880 (1,340–2,460)	3,600 (2,100–4,900)	603
	208 (183–237)	*46.7 (38.4–54.7)*	*86.4 (69.8–108)*	*196 (164–232)*	*443 (363–528)*	*1,030 (792–1,700)*	*1,880 (1,290–2,450)*	
NHW	152 (134–173)	27.2 (20.1–31.1)	52.3 (44.6–61.4)	133 (110–157)	366 (312–450)	977 (796–1,340)	2,470 (1,430–4,330)	907
	149 (133–167)	*31.8 (26.5–34.7)*	*58.6 (50.7–68.6)*	*128 (113–139)*	*313 (249–376)*	*834 (663–1,200)*	*1,950 (1,420–3,350)*	

Abbreviations: MA, Mexican American; NHB, non-Hispanic black; NHW, non-Hispanic white. MEP was detected in all samples.
[a]Italic type denotes measure in µg/g creatinine (95% CI).

Table 2. GM and selected percentiles of MBP concentrations in urine [in µg/L and µg/g creatinine (95% CI)] for the U.S. population ≥ 6 years of age from NHANES 1999–2000.

| | GM | Selected percentiles | | | | | | No. (%) |
		10th	25th	50th	75th	90th	95th	
Total	24.6 (22.7–26.6)	5.70 (4.80–6.40)	12.6 (11.0–14.3)	26.0 (24.2–28.5)	51.6 (46.9–56.1)	98.6 (90.7–114)	149 (126–167)	2,541 (99)
	22.4 (21.1–23.8)[a]	*7.74 (6.79–8.63)*	*12.8 (11.7–14.2)*	*21.9 (20.3–23.4)*	*38.9 (36.1–41.1)*	*68.3 (61.7–74.9)*	*97.5 (84.4–113)*	
Age group (years)								
6–11	41.4 (35.8–47.8)	15.1 (11.0–16.9)	23.0 (19.1–27.2)	40.0 (33.7–50.3)	75.5 (59.0–94.5)	124 (92.8–166)	163 (114–306)	328 (100)
	41.9 (37.2–47.4)	*16.7 (10.6–22.0)*	*27.8 (23.3–32.1)*	*38.9 (32.5–49.6)*	*65.7 (54.9–80.0)*	*107 (80.0–162)*	*159 (106–196)*	
12–19	36.0 (31.9–40.5)	11.9 (8.10–14.8)	20.0 (17.3–25.4)	36.1 (31.7–42.3)	67.7 (56.7–76.1)	119 (94.3–146)	165 (133–209)	752 (100)
	24.3 (22.0–26.8)	*9.80 (7.68–11.5)*	*15.4 (13.2–17.0)*	*23.6 (21.6–26.3)*	*37.6 (32.6–42.2)*	*62.3 (53.7–72.1)*	*88.1 (69.6–139)*	
≥ 20	21.6 (19.7–23.6)	4.70 (4.2–5.9)	10.3 (9.4–11.6)	23.0 (20.7–25.0)	46.1 (39.7–51.3)	95.0 (81.1–107)	142 (118–161)	1,461 (99)
	20.4 (19.0–21.9)	*7.08 (5.95–8.18)*	*11.7 (10.9–13.0)*	*19.5 (18.4–21.0)*	*34.9 (31.2–38.2)*	*62.4 (56.0–68.6)*	*91.0 (78.3–112)*	
20–39	25.1 (21.8–29.0)	6.2 (4.2–7.7)	12.5 (9.8–15.5)	27.7 (23.6–31.7)	50.4 (42.2–55.7)	98.9 (81.6–114)	126 (110–163)	532 (99)
	20.0 (17.9–22.3)	*7.71 (5.27–8.83)*	*12.2 (10.8–14.2)*	*19.1 (17.5–21.3)*	*33.7 (29.1–39.5)*	*56.3 (46.9–69.1)*	*81.4 (60.8–135)*	
≥ 40	19.1 (17.1–21.5)	4.3 (3.4–5.1)	9.4 (8.2–10.5)	19.3 (17.0–22.5)	40.4 (33.8–47.9)	84.4 (67.6–107)	145 (119–170)	929 (98)
	20.7 (19.2–22.4)	*7.06 (5.92–8.27)*	*11.5 (10.3–12.8)*	*19.9 (18.1–22.1)*	*36.4 (31.7–40.1)*	*66.7 (59.1–76.7)*	*97.7 (79.4–115)*	
Sex								
Males	22.0 (20.2–24.0)	5.70 (4.70–6.60)	11.3 (9.90–13.0)	23.1 (21.0–25.2)	43.1 (36.9–49.3)	83.9 (71.3–96.2)	115 (96.2–142)	1,215 (99)
	17.3 (16.0–18.7)	*6.54 (5.70–7.46)*	*10.2 (9.57–11.3)*	*17.0 (15.5–18.7)*	*28.6 (25.8–32.0)*	*49.1 (42.4–53.9)*	*63.6 (57.3–76.7)*	
Females	27.3 (24.4–30.4)	5.80 (4.10–7.60)	13.8 (11.6–16.4)	30.0 (26.1–33.1)	59.5 (52.0–65.6)	119 (100–143)	167 (145–218)	1,326 (98)
	28.6 (26.5–30.9)	*10.6 (8.54–11.7)*	*17.3 (15.9–18.6)*	*28.6 (26.2–30.4)*	*50.6 (44.9–54.2)*	*84.3 (73.5–97.6)*	*131 (98.5–153)*	
Race/ethnicity								
MA	23.4 (20.8–26.4)	5.10 (4.40–6.10)	11.8 (10.1–13.9)	26.3 (23.6–29.2)	48.1 (41.8–54.6)	92.2 (71.9–107)	116 (101–136)	814 (98)
	21.2 (18.9–23.9)	*6.98 (5.23–8.50)*	*12.9 (10.2–14.5)*	*20.0 (18.2–22.8)*	*40.1 (33.7–44.0)*	*63–6 (57.6–70.1)*	*81.6 (73.9–100)*	
NHB	37.0 (32.5–42.1)	10.3 (8.00–14.4)	22.2 (18.2–24.6)	38.7 (34.5–42.6)	78.2 (63.1–86.7)	117 (104–149)	167 (143–192)	603 (99)
	23.9 (21.6–26.4)	*8.51 (6.90–9.92)*	*13.9 (12.4–16.0)*	*25.0 (20.7–27.9)*	*42.2 (36.8–49.3)*	*69.6 (62.6–83.9)*	*94.4 (76.7–108)*	
NHW	21.8 (19.8–24.0)	5.00 (4.20–6.30)	10.6 (9.60–12.5)	23.1 (20.4–26.1)	45.9 (39.1–51.6)	90.2 (75.4–102)	138 (112–161)	911 (98)
	21.3 (19.6–23.2)	*7.16 (6.03–8.54)*	*12.1 (11.1–13.9)*	*20.5 (18.9–22.9)*	*36.4 (32.3–39.6)*	*67.1 (58.1–74.9)*	*97.6 (81.4–135)*	

Abbreviations: MA, Mexican American; NHB, non-Hispanic black; NHW, non-Hispanic white. No. (%) represents sample size and percentage of detection.
[a]Italic type denotes measure in µg/g creatinine (95% CI).

stored cold (2–4°C) or frozen until they were shipped. Samples were analyzed for creatinine using a Beckman Synchron AS/ASTRA clinical analyzer (Beckman Instruments, Inc., Brea, CA) at the University of Minnesota Medical Center. Samples collected for phthalate metabolite measurements were shipped on dry ice to the CDC's National Center for Environmental Health. Urine samples were stored frozen at –20°C until analyzed. The samples were analyzed by isotope dilution high-performance liquid chromatography coupled with tandem mass spectrometry as previously described (Blount et al. 2000a; Silva et al. 2003b). Phthalate urinary concentrations are reported both in micrograms per liter of urine and in micrograms per gram of urinary creatinine. Creatinine adjustment was used to correct for urine dilution (Jackson 1966).

Demographic categories. On the basis of self-reported data, a composite race/ethnicity

Table 3. GM and selected percentiles of MBzP concentrations in urine [in µg/L and µg/g creatinine (95% CI)] for the U.S. population ≥ 6 years of age from NHANES 1999–2000.

| | GM | Selected percentiles | | | | | | No. (%) |
		10th	25th	50th	75th	90th	95th	
Total	15.3 (14.0–16.8)	2.80 (2.30–3.50)	6.90 (6.00–8.20)	17.0 (15.3–18.6)	35.3 (32.8–38.9)	67.1 (56.8–80.7)	103 (90.3–123)	2,541 (97)
	14.0 (13.0–15.0)[a]	*4.41 (3.64–4.75)*	*7.57 (6.89–8.45)*	*13.3 (12.7–14.6)*	*25.1 (23.5–27.0)*	*50.1 (41.4–59.6)*	*77.4 (69.2–88.7)*	
Age group (years)								
6–11	39.4 (34.7–44.8)	9.40 (7.20–13.9)	22.1 (17.2–28.1)	40.3 (34.2–48.6)	82.0 (59.9–90.0)	128 (98.1–214)	214 (107–464)	328 (99)
	40.0 (34.1–46.9)	*12.5 (9.32–18.3)*	*21.7 (19.4–27.2)*	*38.4 (30.3–50.6)*	*73.2 (58.2–89.4)*	*104 (89.4–142)*	*142 (99.8–173)*	
12–19	25.6 (22.7–29.0)	6.30 (5.10–8.10)	13.4 (10.8–15.9)	28.3 (23.0–33.6)	51.1 (43.7–58.5)	87.9 (71.2–106)	125 (100–160)	752 (100)
	17.3 (15.5–19.3)	*6.01 (5.39–7.09)*	*10.6 (8.68–12.3)*	*17.0 (14.9–19.7)*	*28.3 (24.9–32.3)*	*49.7 (41.4–61.7)*	*69.3 (50.1–81.9)*	
≥ 20	12.4 (11.3–13.8)	2.20 (1.80–2.80)	5.80 (5.10–6.40)	13.8 (12.3–15.3)	28.9 (26.5–31.9)	52.0 (45.3–56.8)	86.3 (61.3–103)	1,461 (96)
	11.8 (10.9–12.7)	*3.59 (3.16–4.42)*	*6.67 (6.09–7.46)*	*12.1 (11.3–12.8)*	*20.1 (18.5–23.1)*	*34.3 (30.5–40.8)*	*57.2 (42.5–73.9)*	
20–39	15.8 (13.4–18.5)	3.1 (2.2–4.2)	8.4 (5.9–10.3)	17.1 (14.1–19.9)	34.0 (28.1–39.6)	58.4 (49.3–90.8)	98.4 (63.8–140)	532 (99)
	12.5 (11.0–14.3)	*4.55 (3.21–5.23)*	*7.49 (6.15–8.83)*	*12.6 (11.4–13.3)*	*20.7 (17.7–24.9)*	*35.0 (28.4–49.4)*	*61.1 (36.3–81.4)*	
≥ 40	10.3 (9.1–11.8)	1.9 (1.2–2.4)	4.8 (4.2–5.3)	11.6 (9.8–13.3)	25.2 (21.4–28.0)	45.0 (38.3–52.1)	67.4 (51.0–87.4)	929 (95)
	11.2 (10.2–12.3)	*3.49 (2.90–4.07)*	*6.20 (5.86–6.67)*	*11.6 (10.5–12.6)*	*19.96 (17.8–23.2)*	*33.8 (28.6–41.2)*	*56.8 (36.0–77.4)*	
Sex								
Males	16.2 (14.5–18.0)	3.40 (2.40–4.40)	8.00 (6.00–9.20)	17.7 (15.5–19.4)	35.4 (32.8–38.6)	69.4 (59.9–85.8)	108 (94.0–139)	1,215 (97)
	12.7 (11.6–13.9)	*3.81 (3.26–4.67)*	*6.58 (5.94–7.61)*	*12.3 (11.5–13.1)*	*23.7 (21.5–26.1)*	*44.5 (36.6–53.3)*	*73.5 (57.0–89.4)*	
Females	14.6 (13.0–16.3)	2.40 (1.90–3.10)	6.10 (5.20–7.60)	16.0 (14.2–19.2)	35.8 (31.0–41.0)	63.7 (54.7–74.1)	103 (86.3–116)	1,326 (97)
	15.3 (14.1–16.5)	*4.84 (4.38–5.72)*	*8.73 (7.52–9.63)*	*14.7 (13.3–16.1)*	*25.9 (24.1–29.2)*	*56.4 (41.4–64.3)*	*80.0 (64.8–99.1)*	
Race/ethnicity								
MA	13.9 (11.9–16.4)	2.40 (1.70–3.50)	6.30 (5.20–7.80)	15.7 (12.1–18.0)	33.0 (26.7–37.2)	67.5 (55.9–80.6)	98.3 (80.6–150)	814 (96)
	12.6 (11.2–14.3)	*3.49 (3.00–4.21)*	*6.55 (5.49–7.77)*	*11.9 (10.7–13.5)*	*24.1 (20.8–28.7)*	*46.5 (40.9–54.2)*	*68.1 (55.2–98.8)*	
NHB	23.0 (20.0–26.5)	5.10 (3.70–6.40)	12.3 (10.0–13.7)	23.0 (20.0–27.0)	49.3 (40.1–56.1)	94.0 (79.1–130)	138 (115–233)	603 (99)
	14.8 (13.0–16.9)	*4.93 (3.90–5.88)*	*7.81 (7.12–8.75)*	*13.6 (11.7–15.6)*	*26.9 (21.9–32.4)*	*55.5 (38.7–77.2)*	*86.8 (64.4–99.8)*	
NHW	14.3 (12.7–16.0)	2.50 (1.90–3.20)	6.50 (5.30–8.10)	16.1 (14.3–18.5)	33.9 (30.7–37.5)	58.7 (52.0–71.5)	103 (73.4–116)	911 (97)
	14.0 (12.7–15.3)	*4.42 (3.52–4.77)*	*7.66 (6.47–8.75)*	*13.4 (12.6–15.2)*	*25.2 (23.2–27.3)*	*53.3 (38.6–65.6)*	*77.9 (69.1–90.3)*	

Abbreviations: MA, Mexican American; NHB, non-Hispanic black; NHW, non-Hispanic white. No. (%) represents sample size and percentage of detection.
[a]Italic type denotes measure in µg/g creatinine (95% CI).

Table 4. GM and selected percentiles of MEHP concentrations in urine [in µg/L and µg/g creatinine (95% CI)] for the U.S. population ≥ 6 years of age from NHANES 1999–2000.

| | GM | Selected percentiles | | | | | | No. (%) |
		10th	25th	50th	75th	90th	95th	
Total	3.43 (3.19–3.69)	< LOD	1.20 (< LOD–1.40)	3.20 (2.90–3.50)	7.60 (6.80–8.20)	14.8 (13.6–17.3)	23.8 (19.2–28.6)	2,541 (78)
	3.12 (2.92–3.35)[a]	*< LOD*	*1.52 (1.37–1.69)*	*3.08 (2.81–3.31)*	*5.88 (5.38–6.27)*	*10.8 (9.47–12.9)*	*18.5 (14.0–23.9)*	
Age group (years)								
6–11	5.12 (4.25–6.16)	< LOD	2.40 (1.80–3.10)	4.90 (3.80–5.50)	11.1 (7.70–13.7)	19.0 (13.7–36.1)	34.5 (14.7–130)	328 (87)
	5.19 (4.17–6.45)	*< LOD*	*2.56 (2.05–3.33)*	*5.37 (4.00–6.29)*	*9.11 (7.51–12.1)*	*21.6 (11.6–41.9)*	*41.9 (13.5–86.2)*	
12–19	3.75 (3.30–4.27)	< LOD	1.60 (1.30–1.80)	3.70 (2.90–4.50)	8.10 (6.30–9.60)	15.0 (11.5–20.2)	22.8 (19.5–26.3)	752 (84)
	2.53 (2.21–2.89)	*< LOD*	*1.22 (1.03–1.46)*	*2.31 (2.11–2.60)*	*5.83 (4.42–6.27)*	*9.63 (7.78–11.3)*	*12.1 (11.0–17.3)*	
≥ 20	3.21 (2.95–3.49)	< LOD	< LOD	3.00 (2.60–3.30)	7.20 (6.30–8.10)	14.2 (12.2–16.5)	22.4 (16.8–27.8)	1,461 (76)
	3.03 (2.80–3.29)	*< LOD*	*< LOD*	*2.98 (2.72–3.26)*	*5.55 (4.90–6.04)*	*10.0 (8.60–12.9)*	*17.5 (13.4–22.1)*	
20–39	4.15 (3.65–4.72)	< LOD	1.40 (1.2–1.9)	3.90 (3.3–4.6)	9.4 (8.0–11.5)	17.5 (14.0–23.7)	27.3 (19.7–42.5)	532 (82)
	3.30 (2.93–3.712)	*< LOD*	*1.52 (1.27–1.91)*	*3.25 (2.68–3.63)*	*6.21 (5.29–7.08)*	*13.3 (9.77–15.4)*	*20.9 (14.7–28.4)*	
≥ 40	2.62 (2.38–2.89)	< LOD	< LOD	2.3 (2.0–2.7)	5.3 (4.7–6.3)	11.3 (8.7–13.6)	16.8 (13.6–22.7)	929 (70)
	2.84 (2.59–3.10)	*< LOD*	*1.49 (1.33–1.67)*	*2.82 (2.58–3.10)*	*4.91 (4.45–5.40)*	*8.75 (7.3–10.2)*	*12.9 (10.0–21.6)*	
Sex								
Males	3.68 (3.26–4.15)	< LOD	1.40 (1.20–1.80)	3.40 (2.80–4.10)	8.00 (6.80–9.10)	16.0 (13.8–20.2)	25.3 (18.3–38.3)	1,215 (81)
	2.89 (2.58–3.24)	*< LOD*	*1.33 (1.19–1.52)*	*2.76 (2.37–3.18)*	*5.58 (4.67–6.11)*	*10.3 (8.90–13.5)*	*21.6 (13.3–28.4)*	
Females	3.21 (2.93–3.51)	< LOD	1.20 (< LOD–1.40)	3.00 (2.70–3.50)	7.00 (5.90–8.10)	13.5 (11.4–15.2)	21.6 (17.2–26.0)	1,326 (76)
	3.36 (3.12–3.63)	*< LOD*	*1.82 (1.63–1.99)*	*3.33 (3.00–3.66)*	*6.15 (5.55–6.76)*	*11.1 (9.33–13.5)*	*16.3 (12.9–23.7)*	
Race/ethnicity								
MA	3.49 (3.13–3.88)	< LOD	1.50 (< LOD–1.70)	3.50 (3.00–3.70)	7.00 (5.90–8.60)	13.3 (10.7–19.1)	23.9 (16.4–29.3)	814 (80)
	3.16 (2.77–3.60)	*< LOD*	*1.54 (1.36–1.79)*	*3.15 (2.62–3.74)*	*5.88 (4.92–7.20)*	*11.6 (10.0–12.6)*	*15.7 (12.6–23.1)*	
NHB	4.82 (4.07–5.71)	< LOD	2.50 (1.70–3.00)	5.10 (4.10–5.90)	9.40 (7.80–11.2)	19.5 (14.6–24.5)	29.2 (19.5–39.3)	603 (879)
	3.11 (2.68–3.61)	*< LOD*	*1.68 (1.31–1.98)*	*3.13 (2.62–3.37)*	*5.84 (4.66–7.06)*	*10.2 (8.77–13.6)*	*18.4 (11.8–35.2)*	
NHW	3.16 (2.89–3.46)	< LOD	< LOD	2.70 (2.50–3.10)	7.30 (6.30–8.20)	14.4 (12.2–16.6)	22.4 (16.5–29.3)	911 (75)
	3.09 (2.80–3.41)	*< LOD*	*< LOD*	*3.08 (2.67–3.48)*	*5.87 (5.14–6.67)*	*10.6 (8.74–13.7)*	*20.0 (13.1–27.7)*	

Abbreviations: MA, Mexican American; NHB, non-Hispanic black; NHW, non-Hispanic white. LOD is 1.2 µg/L. No. (%) represents sample size and percentage of detection.
[a]Italic type denotes measure in µg/g creatinine (95% CI).

variable helped define three major race/ethnicity groups: non-Hispanic blacks, non-Hispanic whites, and Mexican Americans. Persons not defined by these three race/ethnicity groups were included only in the total population estimate. During household interviews, age was reported in years at the last birthday. Age categories were 6–11 years (children), 12–19 years (adolescents), and ≥ 20 years of age (adults). For analyses that would allow comparison with previously reported data, the adult age category was further broken down to 20–39 years, to represent reproductive age in women, and ≥ 40 years.

Statistical analysis. Statistical analyses were performed using the statistical software packages SAS (SAS Institute, Cary, NC) and SUDAAN (release 8.0; Research Triangle Institute, Research Triangle Park, NC). SUDAAN incorporates the sample population weights and calculates variance estimates that account for the complex design of NHANES. The survey-specific sample weights were designed specifically for the one-third subset of the full survey. Parametric statistics were computed only for analytes for which the frequency of detection was ≥ 60%.

We calculated the geometric means (GMs) and distribution percentiles for both the volume-based and creatinine-corrected concentrations using the survey sampling weights, which take into account the unequal selection probabilities caused by the cluster design and the planned oversampling of certain subgroups. The analytical limits of detection (LODs) were MEP, 1.0 μg/L; MBP, 0.6 μg/L; MBzP, 0.8 μg/L; MEHP, 1.2 μg/L; mono-cyclohexyl phthalate (MCHP), 0.7 μg/L; mono-*n*-octyl phthalate (MOP), 0.9 μg/L; and mono-3-methyl-5-dimethylhexyl phthalate [monoisononyl phthalate (MINP)], 0.8 μg/L. For concentrations below the LOD, a value equal

to the LOD divided by the square root of 2 was used (Hornung and Reed 1990).

We used an analysis of covariance model to study the effects of several covariates (i.e., sex, race/ethnicity, age, and urinary creatinine) on the log-transformed urinary phthalate metabolite concentrations. This model enabled us to compare the expected least square geometric mean (LSGM) phthalate metabolite levels for selected demographic groups (e.g., male vs. female), which were adjusted statistically so that subjects had comparable levels of all other covariates. We compared and contrasted the LSGMs of demographic groups using only the volume-based concentrations, because creatinine was included as a covariate. The LSGMs normalize phthalate metabolite levels across demographic groups by standardizing for differences in the other covariates. We obtained similar results for GMs of creatinine-corrected concentrations and for LSGMs. We also determined the weighted correlations among the phthalate metabolites by using a weighted regression model. The analyses were considered to be statistically significant when *p* < 0.05, and were considered to be nominally or marginally significant when *p* > 0.05 but *p* < 0.1. Cotinine concentrations of 0.1 μg/L defined the smoking status for LSGM determinations when an interaction existed between phthalate levels and smoking status. When there was an interaction between age group and smoking status, we analyzed only nonsmokers because the number of smokers was relatively small.

Results

The distribution of the four most commonly detected phthalate metabolites in the approximately 2,540 NHANES 1999–2000 samples analyzed are presented in Tables 1–4 and in Figure 1. The creatinine-adjusted GMs for each demographic group are shown in Figure 2.
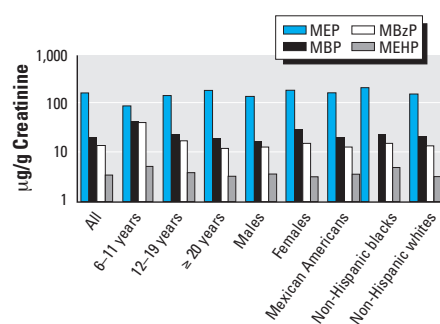
Levels of MEP in the highest concentrations were detected in all of the samples tested. We detected MBP in 99% of the samples, MBzP in 97% of the samples, and MEHP in 78% of the samples tested; however, we found MCHP, MOP, and MINP in < 16% of the samples.

MEP urinary levels by age, sex, and race/ethnicity. The MEP levels by age, sex, and race/ethnicity are displayed in Table 1 and in Figures 2 and 3. We found that MEP creatinine-corrected levels were higher in adults and adolescents than in children. They also were higher in females than in males, and were higher in non-Hispanic blacks compared with non-Hispanic whites and Mexican Americans. The LSGM concentrations of MEP (Table 5) were significantly lower in children than in adolescents (*p* = 0.01753) and adults (*p* < 0.0001); the difference between adult and adolescent LSGM concentrations was only marginally significant (*p* = 0.09296; Table 6). Females had significantly higher LSGM concentrations of MEP than did males (*p* = 0.002). Non-Hispanic blacks had significantly higher LSGM concentrations than did both non-Hispanic whites (*p* = 0.00049) and Mexican Americans (*p* = 0.01788). Mexican Americans had higher concentrations than did non-Hispanic whites, which were marginally significant (*p* = 0.05528; Table 6).

There were significant interactions between age and race/ethnicity (*p* = 0.0244) and between sex and creatinine (*p* = 0.0009). Therefore, age groups were compared separately within each race/ethnicity, and males and females were compared at a common creatinine level of 130.4 mg/dL. Nonsmoking females had significantly higher LSGM MEP concentrations (204.7 μg/L) than did males
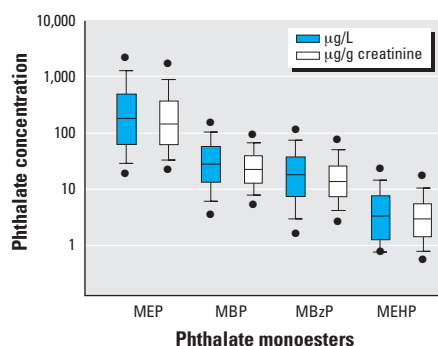
Figure 1. Population distributions of MEP, MBP, MBzP, and MEHP in urine. Circles indicate 5th and 95th percentiles, horizontal bars inside the box indicate the medians, whiskers below and above the 10th and 90th percentiles, and box boundaries are 25th and 75th percentiles. The lower MEHP concentrations compared with MEP, MBP, and MBzP may be due to lower exposure or different pathways, routes of exposure, or pharmacokinetic factors.

Figure 2. GM urinary concentrations (in μg/g creatinine) of MEP, MBP, MBzP, and MEHP in the U.S. general population ≥ 6 years of age. Levels of MEHP, MBzP, and MBP were higher in children than in adolescents and adults. Women had higher levels of MEP, MBzP, and MBP than did males but similar levels of MEHP. Non-Hispanic blacks had higher levels of MEP than did the other race/ethnicity groups.
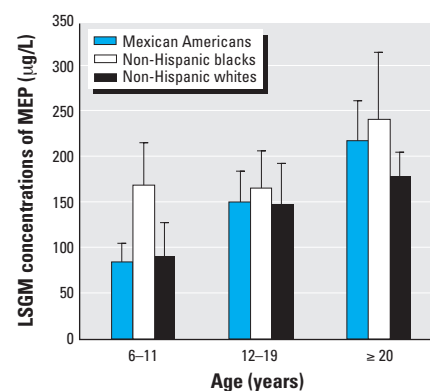
Figure 3. Distribution of MEP levels in urine by age and race/ethnicity (only nonsmokers were used in the LSGM estimation); error bars represent upper 95% CIs. Non-Hispanic blacks had the highest MEP levels. Non-Hispanic black adolescents and adults had higher levels than did non-Hispanic whites and Mexican Americans of the same age group; however, the differences were not significant. MEP levels in non-Hispanic black children were statistically higher than in non-Hispanic white (*p* = 0.00569) and Mexican American (*p* = 0.00035) children.

(149.5 µg/L; $p = 0.01354$). Non-Hispanic blacks had the highest LSGM MEP levels, and adults had higher levels than did adolescents and children (Figure 3). Among nonsmoking non-Hispanic blacks, the LSGM MEP concentrations in adults (243.6 µg/L) were significantly higher than in adolescents (167.1 µg/L; $p = 0.03941$) and higher but not significantly higher than in children (169.3 µg/L; $p = 0.08233$). The differences between children and adolescents were not statistically significant. Among nonsmoking non-Hispanic whites, the LSGM concentrations of MEP in children (91.6 µg/L) were significantly lower than in adolescents (148.0 µg/L, $p = 0.03295$) and adults (178.8 µg/L; $p < 0.00001$); the difference was not significant between adolescents and adults ($p = 0.25460$). Among nonsmoking Mexican Americans, the LSGM concentrations of MEP (Figure 3) in adults (219.6 µg/L) were significantly higher than in children (86.0 µg/L; $p < 0.00001$) and adolescents (152.6 µg/L; $p = 0.00676$). Mexican-American adolescents had significantly higher LSGM MEP concentrations than did Mexican-American children ($p = 0.00021$).

MBP urinary levels by age, sex, and race/ethnicity. The MBP levels by age, sex and race/ethnicity are exhibited in Table 2 and Figure 2. We found that MBP creatinine-corrected levels were higher in children than in adolescents and adults, were higher in females than in males, and were similar among the three race/ethnicity groups. The LSGM MBP concentrations (Tables 5 and 6) in children were significantly higher than in adolescents ($p < 0.00001$) and adults ($p < 0.00001$). Adolescents had significantly higher concentrations than adults ($p = 0.00147$). Furthermore, females had significantly higher concentrations of MBP than did males ($p < 0.00001$). Women of reproductive age (20–39 years of age) had LSGM MBP concentrations (24.4 µg/L) similar

to those of adolescents (34.7 µg/L) and women ≥ 40 years of age (28.6 µg/L; Figure 4). We observed no significant differences among the race/ethnicity groups. Also, we observed no significant interactions between creatinine, age groups, sexes, or race/ethnicities.

MBzP urinary levels by age, sex, and race/ethnicity. The MBzP levels by age, sex, and race/ethnicity are displayed in Table 3 and Figures 2 and 5. We found that MBzP creatinine-corrected levels were higher in children than in adolescents and adults. They also were higher in females than in males and were similar for non-Hispanic whites and non-Hispanic blacks, but were slightly higher in each of these groups than in the Mexican-American group. Children had significantly higher LSGM concentrations of MBzP than did adolescents ($p < 0.00001$) and adults ($p < 0.00001$; Tables 5 and 6). Similarly, adolescents had significantly higher LSGM concentrations of MBzP than did adults. Females had significantly higher LSGM MBzP concentrations than did males ($p = 0.00042$). Non-Hispanic whites had significantly higher LSGM MBzP concentrations than did Mexican Americans ($p = 0.04273$). The differences were not statistically significant between non-Hispanic blacks and both groups of non-Hispanic whites and Mexican Americans (Table 6).

Significant interactions existed between age and sex ($p = 0.0003$), between sex and creatinine ($p = 0.0033$), between race/ethnicity and serum cotinine ($p = 0.0397$), and between age and creatinine ($p = 0.0198$). Because of these interactions, estimates and significance tests were performed within selected groups. LSGM concentrations of MBzP (Figure 5) in female children (46.3 µg/L) were significantly higher than in adult women (14.5 µg/L; $p < 0.00001$) and adolescent girls (18.6 µg/L; $p < 0.00001$); adolescent girls had significantly higher levels than did adult women ($p = 0.01454$).

Similarly, the LSGM concentrations of MBzP (Figure 5) in male children (51.4 µg/L) were significantly higher than in adult men (9.9 µg/L; $p < 0.00001$) and adolescent boys (23.4 µg/L; $p = 0.00006$); adolescent boys had significantly higher levels than did adult men ($p < 0.00001$). Children, regardless of sex, had similar MBzP LSGM levels ($p = 0.46875$). In contrast, adolescent boys and adult men had significantly higher ($p = 0.01814$) and lower ($p = 0.00127$) MBzP LSGM levels, respectively, than did females within the same age group (Figure 5).

MEHP urinary levels by age, sex, and race/ethnicity. The MEHP levels by age, sex, and race/ethnicity are exhibited in Table 4 and Figure 2. We found that MEHP creatinine-corrected levels were higher in children than in adolescents and adults, were higher in females than in males, and were similar among the three race/ethnicity groups. The model-estimated LSGMs of MEHP (Table 5) in children were significantly higher than in adolescents ($p = 0.0001$) and adults ($p = 0.00001$). We observed no statistically significant differences among sex and race/ethnicity groups (Table 6).

Discussion

We measured urinary levels of seven phthalate monoesters in approximately 2,540 NHANES 1999–2000 samples. The detection of MEP, MBP, and MBzP in > 97% and MEHP in > 75% of the samples demonstrates widespread exposure to some phthalates across the U.S. population. We infrequently detected MINP, MOP, and MCHP.

Despite the fact DEHP is the most widely used and produced phthalate, we found higher urinary concentrations of MEP, MBP, and MBzP than of MEHP. The lower MEHP concentrations may be due to lower exposure, absorption, metabolism, or excretion. Metabolism studies of DEHP show that

Table 5. LSGM concentrations of MEP, MBP, MBzP, and MEHP in various demographic groups.

Phthalate metabolite	Ethnicity			Age group			Sex	
	Mexican Americans	Non-Hispanic blacks	Non-Hispanic whites	Children	Adolescents	Adults	Female	Male
MEP	191.9	237.8	162.1	105.2	151.6	187.4	194.4	152.6
MBP	23.0	24.6	23.5	52.2	26.9	21.0	29.8	18.5
MBzP	13.1	14.7	15.5	51.5	19.6	12.5	16.9	13.5
MEHP	3.4	3.6	3.3	5.3	2.9	3.2	3.5	3.2

Table 6. Observed statistical significance values for differences between LSGM concentrations of MEP, MBP, MBzP, and MEHP for various demographic groups.

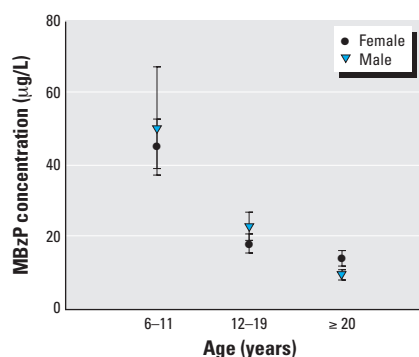| Difference	MEP	MBP	MBzP	MEHP
MA–NHB	0.01788	0.43659	0.25625	0.26329
NHW–NHB	0.00049	0.59064	0.56203	0.26329
MA–NHW	0.05528	0.68315	0.04273	0.47333
Children–adolescents	0.01753	< 0.00001	< 0.00001	0.0001
Adult–adolescents	0.09296	0.00147	< 0.00001	0.31049
Adults–children	< 0.00001	< 0.00001	< 0.00001	0.00001
Female–male	0.002	< 0.00001	0.00042	0.39283

Abbreviations: MA, Mexican Americans; NHB, non-Hispanic blacks; NHW, non-Hispanic whites.
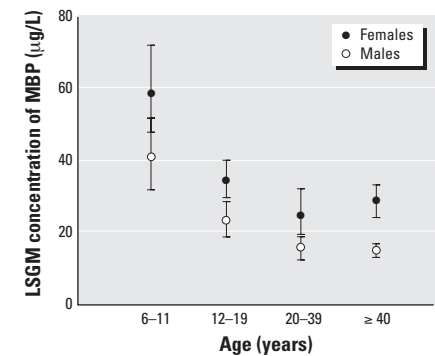
Figure 4. LSGM MBP levels in male and female nonsmoking participants in NHANES 1999–2000. Error bars indicate lower and upper 95% CIs. Females had higher concentrations of MBP than did males, but women of reproductive age had concentrations (24.4 µg/L) similar to those of adolescent girls (34.7 µg/L) and women ≥ 40 years of age (28.6 µg/L).

MEHP undergoes further oxidative metabolism to produce additional metabolites (ATSDR 2002). Recent studies suggest that the urinary concentrations of two of these oxidative metabolites, mono-(2-ethyl-5-oxohexyl) phthalate and mono-(2-ethyl-5-hydroxyhexyl) phthalate are several-fold higher than those for MEHP (Barr et al. 2003; Koch et al. 2003b). Therefore, the relatively low concentrations of MEHP may result, at least in part, from alternative metabolic pathways. A similar metabolism may be important for other long-alkyl-chain phthalates such as dioctyl phthalate (ATSDR 1997) and di-isononyl phthalate (McKee et al. 2002) and might explain the lower frequency and magnitude of detection of their respective monoesters compared with the monoesters of short-alkyl-chain phthalates (e.g., MEP, MBP). The low levels of MCHP found in this population may be due to low exposure to dicyclohexyl phthalate (DCHP), because DCHP is used infrequently in the United States.

The high levels of MEP across the population are most likely associated with the everyday use of consumer products that commonly contain diethyl phthalate (DEP; ATSDR 1995), such as detergents, soaps, cosmetics, shampoo, and perfumes. Furthermore, the higher concentrations of MEP in adults and adolescents than in children are consistent with the known behavioral uses of phthalate-containing consumer products (e.g., adults are more likely to use cosmetics than are children). Concentrations of MEP were highly dependent on both sex and race/ethnicity (Tables 1 and 5). The fact that women had higher concentrations of MEP than did men was most likely attributable to women's increased use of personal care products, such as hair care products, cosmetics, and perfumes. Non-Hispanic black children had LSGM MEP concentrations nearly double

those for non-Hispanic black adolescents and adults, and non-Hispanic blacks had much higher MEP concentrations than did the other two race/ethnicity groups for all ages (Figure 3). We speculate that these differences may be due to increased, continuous, or prolonged use of beauty and hair care products specifically marketed for this population, often beginning at a young age (Figure 3).
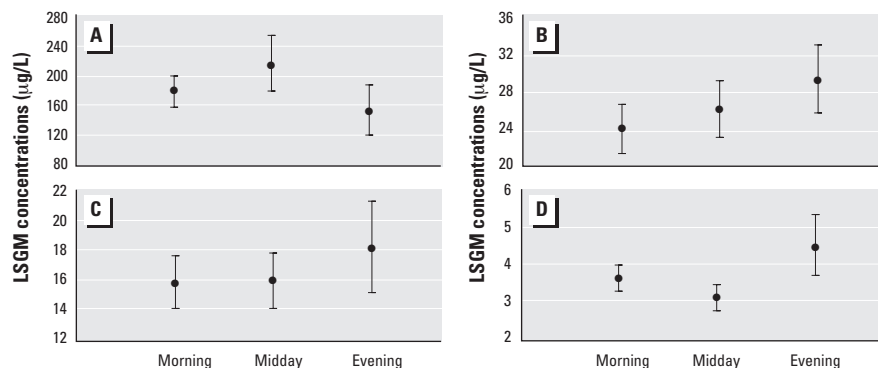
We found that the concentrations of MBzP and MBP were highly correlated (Pearson correlation coefficient $R = 0.62$, $p < 0.0001$). BzBP, the parent phthalate that produces MBzP, can also metabolize to MBP; < 10% of the total BzBP in humans is metabolized to MBP (Anderson et al. 2001). Furthermore, we observed significant correlations between the concentrations of MBP and both MEP ($R = 0.427$, $p < 0.0001$) and MEHP ($R = 0.371$, $p < 0.0001$). These findings suggest a possible common source of exposure for the three parent phthalates; however, the nature of the source is not as apparent as it is for MBzP and MBP.

We observed statistically significant ($p < 0.01$) variations in the population distributions of MEP, MBP, and MEHP depending on the time of sample collection. However, MBzP concentrations did not change significantly. The LSGM concentration of MEP was highest in the midday collection, and the LSGM concentrations of MBP, MBzP, and MEHP were highest in the evening collection (Figure 6). These differences and the nonpersistent nature of phthalates may reflect differences in exposure at different times of the day. For example, a high occurrence of showers and use of personal care products containing DEP in the morning may result in elevated MEP levels in the midday collection samples compared with other collection periods. Similarly, increased contacts with vinyl products such as car seat covers and floor tiles during daytime may result in elevated MEHP levels in the evening collection samples.

We found that the levels of MEHP, MBzP, and MBP were higher in children than

in adolescents and adults (Figure 2). The LSGMs of each of these analytes in children were nearly double those for adolescents and adults (Table 5), suggesting that children have higher levels of exposure to several phthalates. These data are of particular concern because of the known animal toxicity and/or carcinogenicity of DBP, DEHP, and their monoester metabolites (ATSDR 2001, 2002), although at concentrations much higher than those found in this population and because of the increased vulnerability of children. The higher exposure of children to these chemicals may be reasonably explained because of their higher food consumption and air inhalation in relation to their weight compared with those of adolescents or adults. In addition, children typically spend more time indoors, and some toys may contain high concentrations of plasticizers. However, the observed differences could be related to other variables, such as differences in absorption, distribution, metabolism, or excretion of these phthalates. Nevertheless, our findings highlight the need for additional toxicokinetic information on phthalates, especially in children, and the need for epidemiologic studies to target health outcomes related to phthalate exposures in children.

We previously reported phthalate monoester concentrations in a convenience group of 289 samples from the NHANES III callback cohort (Blount et al. 2000b). NHANES III (1988–1994) was designed as a nationally representative survey, but the environmental component, known as the callback cohort (composed of ~1,000 adults who agreed to have additional blood and urine samples taken) was not. Although each demographic group had some representation in the callback cohort, no rigorous sample design and no sample weights were used in analyzing the resulting data. The frequencies of detection of the phthalate monoesters were similar among NHANES III and NHANES 1999–2000. However, the GMs and medians of the three most frequently detected phthalate metabolites, MEP, MBP, and MBzP, were almost 2-fold lower in the

Figure 5. LSGM MBzP levels in male and female nonsmoking participants in NHANES 1999–2000. Error bars indicate lower and upper 95% CIs. Children had the highest levels: levels in female children were significantly higher than in adult women ($p < 0.00001$) and adolescent girls ($p < 0.00001$); similarly, the concentrations in male children were significantly higher than in adult men ($p < 0.00001$) and adolescent boys ($p = 0.00006$).

Figure 6. LSGM concentrations of (A) MEP, (B) MBP, (C) MBzP, and (D) MEHP for each daily examination period. Error bars represent lower and upper 95% CIs. The concentration of MEP was highest in the midday collection. In contrast, the concentrations of MBP, MBzP, and MEHP were highest in the evening collection.

NHANES 1999–2000 population than in the NHANES III study population, whereas the MEHP concentrations remained essentially constant. These findings may be due to reduced exposures or may reflect differences among sample populations. Compared with the NHANES III study population (Blount et al. 2000b), women of reproductive age (20–39 years of age) had concentrations of MBP similar to those of women 40 or more years of age in the NHANES 1999–2000 population (Figure 4). These findings are important because DBP is a reproductive toxicant; however, women still continue to have higher MBP concentrations than do men. The increased levels of MBP among women 20 to 39 years of age observed in the small subset of NHANES III samples is likely related to the small sample size and nonrepresentative nature of the sampling (Blount et al. 2000b). However, it is possible that a true decrease in exposure to DBP for women in this age group may have occurred since the NHANES III sampling. Although the two data sets are not directly comparable for establishing exposure trends over time, the NHANES III data provided useful exposure information to help focus research efforts.

The phthalate monoester data in specific study populations reported in the literature are limited. Hoppin et al. (2002) evaluated the temporal variability of urinary phthalate monoester concentrations in two consecutive first morning voids from 46 African-American women in the Washington, DC, area that were collected during 1996–1997. The authors reported frequent detection of MEP, MBzP, MBP, and MEHP as well as reasonably stable concentrations between the 2 days. The median concentrations of MEP (211 µg/L) were similar to our NHANES 1999–2000 data even compared with data from all individual demographic categories that applied (i.e., adults, women, non-Hispanic blacks). However, the median concentrations of MBzP (31 µg/L), MBP (52 µg/L), and MEHP (7.3 µg/L) in the 46 African-American women were consistently 1.5–2 times higher than the NHANES 1999–2000 data, regardless of the demographic category used for comparison.

In a similar study conducted in New York City, the same monoester metabolites were frequently detected in 25 urine samples collected from pregnant African-American and Dominican women (Adibi et al. 2003). The median MBzP concentration (12.1 µg/g creatinine) of this group was similar to that measured here for several demographic groups, including adults, women, non-Hispanic blacks, and Mexican Americans. Also, median concentrations of MEP (236 µg/L) and MEHP (4.6 µg/L) were somewhat higher than for the NHANES 1999–2000 population groups. The median concentration of MBP

(42.6 µg/L) was 1.5–2 times higher than the NHANES 1999–2000 levels, both collectively and compared with the demographic groups. Because reproductive toxicity has been demonstrated in pregnant rodents exposed to high doses of DBP, this population should be studied further to evaluate any associated health end points.

Phthalate monoester concentrations also have been measured in 168 men, most of whom were non-Hispanic whites, to determine if a relation existed between sperm DNA damage and phthalate exposure (Duty et al. 2003). The specific gravity-adjusted GM concentrations of MEP (187 µg/L) and MBP (18.2 µg/L) of these men were similar to those of the adults, men, and non-Hispanic whites in our study population. The GM MBzP concentration in the 168 men was about half of that found in the NHANES 1999–2000 population, but MEHP concentrations were about double of those we found for our total population and the relevant demographic groups.

In another study, phthalate monoester concentrations were measured in 19 toddlers 12–18 months of age in Imperial Valley, California (Brock et al. 2002). Similar to results of other studies, the metabolites predominantly detected were MEP, MBP, MBzP, and MEHP. Although a comparable age group was not included in the NHANES 1999–2000 population, we compared these 19 toddler metabolite concentrations with those of children 6–11 years of age in NHANES 1999–2000. The unadjusted mean concentrations of MEP and MBP were approximately two and three times higher, respectively, than the GM concentrations in NHANES 1999–2000, whereas the mean concentrations of MBzP and MEHP were similar.

A recent study has reported the levels of several phthalate monoesters (including MEP, MBP, and MEHP) in eight nonoccupationally exposed individuals in Germany (Koch et al. 2003a). The mean levels of MEP (1,000 µg/L), MEHP (8.87 µg/L), and MBP (36.5 µg/L) were significantly higher than the levels found in the NHANES 1999–2000 population, but the MBzP levels (7.2 µg/L) were about half the value found in our present study. The same group of investigators also measured the concentrations of the same phthalate metabolites in the first morning voids, which were collected in April 2002, from 53 females and 32 males, 7–64 years of age, who live in southern Germany (Koch et al. 2003b). Similar to the results for the NHANES 1999–2000 population, females had higher creatinine-adjusted urinary levels of MEP, MBP, MBzP, and MEHP than did males. These data suggest similar sex-related differences in exposure to phthalates both in the United States and in Germany. However, the median levels of MBP (157 µg/g creatinine) were 8-fold higher and

the median levels of MEHP (9.2 µg/g creatinine) were 3-fold higher in the German population than in the NHANES 1999–2000 population. Concentrations of MEP (73.3 µg/g creatinine) were about half those found in NHANES 1999–2000, but levels of MBzP (17.2 µg/g creatinine) were similar. These data suggest that differences in the exposure to phthalates may exist geographically. Also, the varying amounts of phthalates used and sampling times (e.g., first morning voids vs. non-first morning voids, seasonal vs. throughout-the-year collection) may account for the observed differences in the levels of urinary phthalates.

Conclusions

We report the first nationally representative population-based phthalate monoester concentrations for selected demographic groups in the United States. These data can be used with future 2-year surveys to evaluate trends in phthalate exposure. Consistent with our previous results, we found that exposure to phthalates in the United States is widespread. We found measurable concentrations of MEP, MBP, and MBzP in > 97% of the samples tested but found three other metabolites (MCHP, MOP, and MINP) in < 20% of the samples tested. In addition, we saw significant differences in metabolite concentrations across the demographic groups. Children 6–12 years of age had higher concentrations of MBP, MBzP, and MEHP, whereas adults had higher concentrations of MEP than did children. Non-Hispanic blacks had significantly higher concentrations of MEP than did other race/ethnicity groups. Females had higher concentrations of MBP, the metabolite of the reproductive toxicant DBP, than did males; however, women of reproductive age had concentrations of MBP similar to those of women ≥ 40 years of age. Collectively, these data highlight the need for additional research to evaluate human health effects that result in high levels of exposures to DEP, DBP, BzBP, DEHP, and other phthalates.

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