

Urinary Biomarkers of Exposure to Jet Fuel (JP-8)

Berrin Serdar,¹ Peter P. Egeghy,¹ Suramya Waidyanatha,¹ Roger Gibson,² and Stephen M. Rappaport¹

¹Department of Environmental Sciences and Engineering, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA; ²Office of the Assistant Secretary of Defense (Health Affairs), Clinical and Program Policy, Falls Church, Virginia, USA

Benzene, naphthalene, and 1- and 2-naphthol were measured in urine samples obtained from 322 U.S. Air Force personnel categorized *a priori* as likely to have low, moderate, or high exposure to jet fuel [jet propulsion fuel-8 (JP-8)]. In postexposure samples, levels of these analytes in the high-exposure group were 3- to 29-fold greater than in the low-exposure group and 2- to 12-fold greater than in the moderate-exposure group. Heavy exposure to JP-8 contributed roughly the same amount of benzene and more than three times the amount of naphthalene compared with cigarette smoking. Strong correlations were observed among postexposure levels of naphthalene-based biomarkers in urine and naphthalene in air and breath. We conclude that urinary naphthalene and the naphthols can serve as biomarkers of exposure to jet fuel. Of these, the naphthols are probably more useful because of their greater abundance and slower elimination kinetics. *Key words:* benzene, biomarkers, exposure assessment, jet fuel, JP-8, naphthalene, naphthols, urine. *Environ Health Perspect* 111:1760–1764 (2003). doi:10.1289/ehp.6275 available via <http://dx.doi.org/> [Online 2 July 2003]

Jet propulsion fuel-8 (JP-8) is the primary jet fuel used by the U.S. Air Force and other members of the North Atlantic Treaty Organization (NATO), which collectively consume an estimated 20 billion liters per year (Zeiger and Smith 1998). Over the last 20 years, JP-8 has completely replaced jet propulsion fuel-4 (JP-4) in the U.S. Air Force because of a desire to move toward a single battlefield fuel and because its higher flash point and lower vapor pressure make it less likely to propagate an explosion. JP-8 is a kerosene-based fuel consisting of approximately 81% aliphatic hydrocarbons and 19% aromatic hydrocarbons (Carlton and Smith 2000; White 1999; Zeiger and Smith 1998). The worldwide annual use of kerosene-based jet fuels, which includes Jet-A, the commercial airline equivalent of JP-8, is estimated at around 240 billion liters (Ritchie et al. 2001).

Little is known about exposures to JP-8 or about possible health effects associated with exposures. Based upon limited toxicologic data, it has been speculated that workers exposed to JP-8 are at increased risk of respiratory, cardiovascular, and neurologic effects (ATSDR 1998; Knave et al. 1976; Porter 1990; Ritchie et al. 2001; Struwe et al. 1983). Because JP-8 is irritating to the skin (Kanikkannan et al. 2001; McDougal and Robinson 2002) and because kerosene (the base mixture of hydrocarbons in JP-8) has caused skin cancer in mice (NTP 1986), dermal contact with this fuel is also worrisome.

Although exposure to JP-8 can occur at any stage in the transport or use of jet fuel, the highest levels are thought to occur during maintenance of aircraft fuel tanks, where fuel vapors can accumulate, despite venting before entry (Carlton and Smith 2000). The risk of dermal exposure is also great during fuel-tank

maintenance because personnel must first remove fuel and fire-suppressing foam from the aircraft and, ultimately, enter the confines of the tanks where residual fuel remains. (At the time this study was conducted, Air Force fuel-tank workers wore only cotton garments to prevent static electricity.)

Given the myriad of chemicals comprising jet fuel, assessing exposures to JP-8 has been problematic. Several aliphatic and aromatic hydrocarbons, including C₉ to C₁₂ *n*-alkanes, benzene, toluene, styrene, and naphthalene, have been proposed as possible surrogates of JP-8 exposure, based upon parallel measurements in breathing-zone air and breath (Carlton and Smith 2000; Egeghy et al. In press; Pleil et al. 2000; Puhala et al. 1997). Of these, the aromatic compounds tend to be more hazardous, with benzene being arguably the most toxic constituent of jet fuel, because of its well-recognized hematopoietic and carcinogenic effects (IARC 1982; IPCS 1993). However, although benzene is a minor component of JP-8, typically present at much less than 0.02% (Carlton and Smith 2000; IARC 1989; Irwin et al. 1997), it is abundant in cigarette smoke and gasoline exhaust (IARC 1989; Rustemeier et al. 2002). Also, because of the great volatility of benzene (as with toluene, styrene, and the other of single-ring aromatic compounds), exposure occurs almost exclusively via inhalation, with very little dermal absorption. For these reasons, benzene is unlikely to be a good surrogate for JP-8 exposure, even though it is reasonable to assess exposure to benzene *per se* among persons exposed to jet fuel.

Naphthalene is an abundant aromatic constituent of JP-8 (IARC 1989; White 1999), present at 0.175% in batches of JP-8 from the present study (Egeghy et al. In

press). Unlike benzene, naphthalene is readily absorbed into the blood via both inhalation and dermal contact (McDougal and Robinson 2002; NTP 2000) and is only a minor component of cigarette smoke and gasoline exhaust (IARC 1989; Rustemeier et al. 2002). Thus, naphthalene could be a good surrogate for JP-8 exposure, and naphthalene-based biomarkers could be particularly useful in assessing whole-body exposures to jet fuel as the prelude to studies of health effects.

After exposure, some of the naphthalene dose is eliminated unchanged in the breath or urine. However, most of the naphthalene dose is metabolized via cytochrome P450 enzymes (CYP1A1, CYP1A2, CYP2A1, CYP2E1, CYP2F1, CYP2F2, CYP3A5, and CYP3A7) to naphthalene-1,2-epoxide, which rearranges to 1- and 2-naphthol (Greene et al. 2000; Tingle et al. 1993; Wilson et al. 1996); these products are excreted in the urine, either unchanged or after conjugation (NTP 2000). Although recent reports have suggested that the naphthols might be useful biomarkers of exposure to polycyclic aromatic hydrocarbons (naphthalene is the simplest such compound; Bouchard et al. 2001; Jansen et al. 1995; Yang et al. 1999), here we consider the potential of naphthols as candidates for biomonitoring of JP-8.

In this study, we measured levels of unmetabolized benzene and naphthalene and of 1- and 2-naphthol in the urine of 323 Air Force personnel. We then compared the levels of these urinary analytes after *a priori* categorization of subjects by exposure level (low, moderate, and high) and by smoking status. We subsequently investigated the correlations

Address correspondence to S.M. Rappaport, Department of Environmental Sciences and Engineering, School of Public Health, University of North Carolina, Chapel Hill, NC 27599-7431, USA. Telephone: (919) 966-5017. Fax: (919) 966-0521. E-mail: smr@unc.edu

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of the urinary analytes and the corresponding air and breath levels of benzene and naphthalene in these subjects.

Materials and Methods

Chemicals and supplies. Naphthalene ($\geq 99\%$, scintillation grade), [$^2\text{H}_8$]naphthalene (≥ 98 atom% D), 1-naphthol ($\geq 99\%$), 2-naphthol ($\geq 99\%$), [$^2\text{H}_7$]1-naphthol (97 atom% D), [$^2\text{H}_6$]benzene, and methanol (purge and trap grade) were obtained from Aldrich Chemical Co. (Milwaukee, WI). Benzene was obtained from Fluka Chemical Co. (St. Gallen, Switzerland). NaCl was obtained from Fisher Scientific (Pittsburgh, PA). β -Glucuronidase/sulfatase (type H-2 from *Helix pomatia*; β -glucuronidase activity, 105,000 U/mL; sulfatase activity, 4,300 U/mL) was obtained from Sigma Chemical Co. (St. Louis, MO). Tri-Sil TBT was obtained from Pierce Chemical (Rockford, IL). Ethyl acetate (analytical reagent) and hexane (nanograde) were obtained from Mallinckrodt Baker, Inc. (Paris, KY).

Study subjects and sampling. Spot urine samples were collected from 323 active duty Air Force personnel (on six Air Force bases in the United States) before and after a 4-hr work shift (measurements of one subject were excluded from statistical analyses, as described below). Urine samples were collected in 15-mL polyethylene tubes in the field and shipped on dry ice to the laboratory, where they were stored at -80°C until analysis.

Briefings, press releases, and solicitation advertisements were used to recruit study volunteers. Subjects were recruited with informed consent from both sexes (272 males, 51 females) according to their job titles (primary career fields) and were categorized into low-, moderate-, and high-exposure groups based on the anticipated likelihood of JP-8 exposure in their jobs. Aircraft fuel-system maintenance workers (jobs: entrant, attendant, runner, and multiple jobs) were assigned to the high-exposure group. The moderate-exposure group consisted of workers who did not perform fuel tank maintenance but whose work involved regular contact with jet fuel (jobs: fuel handling, distribution, etc.). The low-exposure group consisted of personnel whose job titles covered a wide variety of activities that did not require exposure to jet fuel (jobs: military police, medical technician, and the like). Information about smoking status was obtained by questionnaire. Subjects who smoked were asked to abstain for the duration of the 4-hr study period. The numbers of subjects categorized by exposure group and smoking status are summarized in Table 1.

Urinary measurements of one participant were excluded from all statistical analyses. Although this person was categorized in the low-exposure group, he reported being in the

hangar with aircraft fuel maintenance workers and showed high levels of exposure (benzene, $4.80 \mu\text{g}/\text{m}^3$; naphthalene, $482 \mu\text{g}/\text{m}^3$) compared with the other subjects in the low-exposure group [geometric means (GMs): benzene, $3.25 \mu\text{g}/\text{m}^3$; naphthalene, $2.11 \mu\text{g}/\text{m}^3$].

Analysis of urinary analytes. Urinary benzene, naphthalene, and 1- and 2-naphthol were measured in all postexposure samples ($n = 323$) and in about half of the preexposure samples ($n = 152$). Unmetabolized benzene and naphthalene were determined in urine via headspace solid-phase microextraction based upon the method of Waidyanatha et al. (2001) using a Varian Model 8200 autosampler (Walnut Creek, CA) with an Autotherm Peltier controller and carousel (Strument Scientific, Padova, Italy). Briefly, 0.5 mL urine was transferred to a vial containing 0.5 g NaCl to which 1 μL of a methanol solution of internal standards, containing 0.5 $\mu\text{g}/\text{mL}$ [$^2\text{H}_8$]naphthalene and 2.5 $\mu\text{g}/\text{mL}$ [$^2\text{H}_6$]benzene, was added. The vials were immediately capped and placed in the carousel at 45°C for 15 min to allow the analytes to equilibrate. Analytes were concentrated from the vial headspace onto a Supelco (Bellefonte, PA) polydimethylsiloxane fiber (10-mm \times 100- μm film thickness) for 15 min and were then analyzed by gas chromatography-mass spectrometry (GC-MS) in selected ion monitoring (SIM) mode using a Hewlett-Packard 5980 series II gas chromatograph coupled to an HP 5971 A mass selective detector (Hewlett Packard, Palo Alto, CA). A DB-5 fused silica capillary column was used (60 m, 0.25-mm inner diameter, 0.25- μm film thickness). Ions at m/z 128 (naphthalene), 136 ([$^2\text{H}_8$]naphthalene), 78 (benzene), and 84 ([$^2\text{H}_6$]benzene) were monitored. Quantitation was based on peak area ratios of the analytes to the internal standards. Preexposure benzene was not quantified in one urine sample (low-exposure group) because of chromatographic difficulties.

Urinary 1- and 2-naphthol levels were measured as described by Serdar et al. (2003). Briefly, 2 mL urine was brought to room temperature and 50 μL of a hexane solution containing 1 $\mu\text{g}/\text{mL}$ of [$^2\text{H}_7$]1-naphthol (internal standard) was added. The sample was hydrolyzed with 10 μL β -glucuronidase/sulfatase at 37°C for 17 hr and extracted twice with a total of 7 mL ethyl acetate. After evaporation under N_2 , the residue was derivatized with 10 μL Tri-Sil TBT in 190 μL hexane at 70°C for 30 min. The trimethylsilyl ethers of the analytes were then analyzed by GC-MS in SIM mode. Molecular ions at m/z 216 (1- and 2-naphthol), m/z 223 ([$^2\text{H}_7$]1-naphthol) were monitored, and the quantitation was based on peak area ratios of the naphthols to [$^2\text{H}_7$]1-naphthol.

Adjustment for urinary creatinine. Levels of urinary creatinine in our samples were

provided by another laboratory, which performed the assays with a Vitros 250 Chemistry System (Ortho-Clinical Diagnostics, Rochester, NY). Only urinary naphthols were adjusted for creatinine, and all statistical tests were repeated with and without adjustment. Because only minor differences were observed with and without adjustment for creatinine (summarized in "Results"), only unadjusted levels of the naphthols are reported herein. Unmetabolized benzene and naphthalene were not adjusted for creatinine because, unlike creatinine, which is eliminated through glomerular filtration and is not reabsorbed, they are excreted into urine through a concentration-dependent passive process that involves tubular reabsorption (Boeniger et al. 1993; Waidyanatha et al. 2001).

Analysis of benzene and naphthalene in air and breath. Personal exposure to benzene and naphthalene was monitored during the 4-hr work shift with passive monitors clipped to the subject's clothing in the breathing zone. End-exhaled air samples were collected from each subject before and after the work shift using 75-cm³ glass bulbs. Details of the collection and analysis of benzene and naphthalene in air and breath samples are presented elsewhere (Egghy et al. In press).

Statistical analyses. Multiple comparisons were applied to test for the differences in mean (log-transformed) levels of urinary biomarkers (before and after the exposure) categorized by work category and cigarette smoking status. For this purpose, a two-way analysis of variance (ANOVA) procedure was applied via Proc GLM of SAS system software (version 8.1; SAS Institute, Cary, NC). GM levels of urinary analytes in samples collected before and after exposure were compared using Student's t -tests of the logged values (Proc t -test; SAS). Spearman correlation coefficients were obtained for pairs of measurements in urine, air, and breath. All statistical analyses were performed using SAS at a significance level (two-tailed) of 0.05. All tests (except Spearman correlation) were performed after (natural) logarithmic transformation, and data were summarized as GMs and geometric standard deviations (GSDs). A small proportion of measurements of urinary benzene ($n = 1$ in a postexposure sample) and naphthalene ($n = 10$ in preexposure and $n = 15$ in postexposure

Table 1. Distribution of study participants by exposure group (n) and smoking status.

Smoking status, sex	Exposure group (n)		
	Low	Moderate	High
Nonsmokers			
Female	26	3	4
Male	90	17	62
Smokers			
Female	12	2	4
Male	38	17	47

samples) measurements were below the limit of detection (LOD); these samples were assigned a value of LOD/√2 before statistical analysis (Reed 1990).

Results

Effects of exposure category and smoking status.

Tables 2 and 3 present summary statistics of benzene, naphthalene, and 1- and 2-naphthol in urine samples collected, respectively, before and after the work shift from subjects classified by exposure category and smoking status. Regarding the preexposure levels, GM levels of urinary analytes were not different across exposure groups, except for 1-naphthol, which was 2-fold higher in the high-exposure group than in the low-exposure group ($p < 0.05$). However, smokers had significantly higher preexposure levels of all urinary analytes than nonsmokers except for naphthalene, where statistical significance was approached ($p < 0.1$)

only in the low- and the high-exposure groups (Table 2). Regarding postexposure levels (Table 3), concentrations of all urinary analytes in the high-exposure group were 3- to 28-fold higher than those of the low-exposure group and 2- to 12-fold higher than those of the moderate-exposure group. Concentrations of naphthalene and the naphthols were also 2-fold higher in the moderate-exposure group than the low-exposure group. Smokers had significantly higher levels than nonsmokers of postexposure samples of all analytes except naphthalene (Table 3).

When levels of urinary analytes were compared between pre- and postexposure samples within a given exposure category, postexposure levels of all analytes were significantly greater in the high-exposure group, but not in the low- or moderate-exposure groups.

Correlations among measurements in urine, breath, and air. Spearman correlation

coefficients are shown in Tables 4 and 5 for preexposure and postexposure samples, respectively, for all urinary analytes as well as for benzene and naphthalene in breathing-zone air and breath. All coefficients were significant except those involving naphthalene in the breath of preexposed subjects. Postexposure urinary measurements showed much larger correlation with measurements in breath ($r = 0.366$ – 0.613) and urine ($r = 0.517$ – 0.896) than did those for the corresponding preexposure samples ($r = -0.035$ to 0.397 and $r = 0.343$ – 0.784 , respectively). The correlation coefficients between levels of naphthalene and 1- and 2-naphthols diminished by 30.2 and 38.3%, respectively, in pre-exposure samples and by 14.7 and 11.9%, respectively, in postexposure samples when naphthols were adjusted for urinary creatinine (data not shown).

Discussion

JP-8 exposure is believed to be the most common chemical exposure experienced by Air Force personnel, and similar exposures are expected among workers at commercial airlines from Jet-A. Despite the common exposures worldwide and speculation that JP-8 might be associated with adverse health effects (ATSDR 1998; Ritchie et al. 2001), very few investigations have monitored exposures to constituents of jet fuel. In the present study, we investigated levels of benzene, naphthalene, and 1- and 2-naphthol in the urine of smoking and nonsmoking workers expected to have low, moderate, and high exposure to JP-8.

Our primary aim was to determine whether naphthalene and its biomarkers might be useful surrogates for JP-8 in studies of health effects associated with exposure to jet fuel. We observed much lower levels of naphthalene in urine than those of the naphthols, which is not surprising because relatively small amounts (< 1–2%) of unmetabolized aromatic compounds are eliminated in urine (Ghittori et al. 1993; Parke 1996; Turkall et al. 1994). When we aggregated postexposure levels of urinary naphthalene and 1- and 2-naphthol by exposure category, the values supported the *a priori* categorization based upon job title (Table 3). Levels of naphthalene, and 1- and 2-naphthol were approximately 28-, 13-, and 10-fold higher, respectively, in postexposure urine samples in the highest category compared with the lowest category. This suggests that the urinary biomarkers of naphthalene did indeed track the extent to which subjects in the selected jobs were thought to have contact with JP-8.

In the present study, postexposure levels of urinary 1- and 2-naphthols in the low-exposed group were comparable with previously reported mean values in control populations, as summarized in Table 6. Levels of postexposure urinary 1- and 2-naphthol in workers with heavy JP-8 exposures (19.8 and 28.1 µg/L,

Table 2. Preshift urinary measurements among controls and U.S. Air Force personnel exposed to JP-8.

Urinary analyte	Low		Moderate		High	
	NS (n = 48)	S (n = 26)	NS (n = 8)	S (n = 8)	NS (n = 36)	S (n = 26)
Benzene	0.554 ^a (1.55)	2.10*(3.32)	0.568 (1.83)	3.13*(3.33)	0.709 (1.90)	1.72*(2.58)
Naphthalene	0.014 (4.79)	0.027 ^a (2.46)	0.025 (3.20)	0.032 (1.68)	0.016 (6.51)	0.033 ^a (2.80)
1-Naphthol	1.19 (3.16)	3.98*(2.63)	1.85 (2.36)	5.52** (1.61)	2.04 (3.24)	7.76*(3.10)
2-Naphthol	2.06 (2.75)	7.55*(2.60)	2.10 (2.10)	7.77** (1.52)	2.06 (2.27)	9.49*(2.54)

Abbreviations: NS, nonsmokers; S, smokers. GMs (µg/L) and GSDs (in parentheses) are shown by exposure category and smoking status.

^an = 47. * $p < 0.0001$; ** $p < 0.05$; ^a $p < 0.1$ for test of equal GMs against the nonsmokers within the exposure category (two-way ANOVA of log-transformed data).

Table 3. Postshift urinary measurements among controls and U.S. Air Force personnel exposed to JP-8.

Urinary analyte	Low		Moderate		High	
	NS (n = 116)	S (n = 50)	NS (n = 20)	S (n = 19)	NS (n = 66)	S (n = 51)
Benzene	0.695 (1.64)	1.60*(2.60)	0.675 (1.52)	2.56*(2.78)	1.81 (2.80)	3.71*(3.40)
Naphthalene	0.014 (4.08)	0.012 (4.71)	0.025 (2.68)	0.040 (2.09)	0.316 (11.2)	0.457 (4.93)
1-Naphthol	0.945 (2.59)	4.24*(2.79)	1.57 (2.87)	6.44*(2.35)	15.9 (3.21)	26.3** (2.32)
2-Naphthol	1.77 (2.72)	7.20*(3.21)	3.78 (2.81)	10.7** (2.54)	22.6 (3.46)	37.3** (2.48)

Abbreviations: NS, nonsmokers; S, smokers. GMs (µg/L) and GSDs (in parentheses) are shown by exposure category and smoking status.

* $p < 0.0001$, ** $p < 0.05$ for test of equal GMs against the nonsmokers within the exposure category (two-way ANOVA of logged data).

Table 4. Correlation among biomarkers in urine (µg/L) and breath (µg/m³) in preexposure samples of all subjects [Spearman coefficients (p-value)].

	Benzene (urine)	Naphthalene (urine)	1-Naphthol (urine)	2-Naphthol (urine)
Benzene (breath)	0.397 (< 0.0001)	0.202 (0.013)	0.345 (< 0.0001)	0.356 (< 0.0001)
Naphthalene (breath)	-0.084 (0.313)	0.135 (0.100)	-0.035 (0.671)	-0.072 (0.385)
Benzene (urine)		0.343 (< 0.0001)	0.550 (< 0.0001)	0.607 (< 0.0001)
Naphthalene (urine)			0.482 (< 0.0001)	0.397 (< 0.0001)
1-Naphthol (urine)				0.784 (< 0.0001)

Table 5. Correlation among exposure measurements (air; µg/m³) and biomarkers in urine (µg/L) and breath (µg/m³) in postexposure samples of all subjects [Spearman coefficients (p-value)].

	Benzene (urine)	Naphthalene (urine)	1-Naphthol (urine)	2-Naphthol (urine)
Benzene (breath)	0.589 (< 0.0001)	0.455 (< 0.0001)	0.613 (< 0.0001)	0.575 (< 0.0001)
Naphthalene (breath)	0.366 (< 0.0001)	0.478 (< 0.0001)	0.552 (< 0.0001)	0.508 (< 0.0001)
Benzene (air)	0.476 (< 0.0001)	0.659 (< 0.0001)	0.721 (< 0.0001)	0.689 (< 0.0001)
Naphthalene (air)	0.461 (< 0.0001)	0.692 (< 0.0001)	0.720 (< 0.0001)	0.694 (< 0.0001)
Benzene (urine)		0.517 (< 0.0001)	0.643 (< 0.0001)	0.645 (< 0.0001)
Naphthalene (urine)			0.690 (< 0.0001)	0.648 (< 0.0001)
1-Naphthol (urine)				0.896 (< 0.0001)

Table 6. GM levels of urinary biomarkers ($\mu\text{g/L}$) in control populations (GSDs in parentheses).

Author (year)	Country	Sample size		Benzene		1-Naphthol		2-Naphthol	
		NS	S	NS	S	NS	S	NS	S
Yang et al. (1999)	Japan	34	38	—	—	3.00 (5.6)	8.30 (3.6)	1.10 (4.9)	7.80 (3.6)
Nan et al. (2001)	Korea	87	41	—	—	—	—	2.45 ^a (3.46)	6.22 ^a (2.99)
Bouchard et al. (2001)	Canada ^b	25	—	—	—	1.51 ^c	—	1.40 ^c	—
Serdar et al. (2003)	China	19	3	—	—	3.22 (2.22)	14.7 (1.44)	3.29 (1.99)	19.1 (1.51)
Ghittori et al. (1993)	Italy	20	20	0.131 (0.002)	0.790 (0.002)	—	—	—	—
Kok and Ong (1994)	Singapore	25	50	0.09 (0.002)	0.339 (0.002)	—	—	—	—
Waidyanatha et al. (2001)	China	23	17	0.116 (0.172)	0.191 (0.486)	—	—	—	—
Present study ^d	U.S.	116	50	0.695 (1.64)	1.60 (2.60)	0.945 (2.59)	4.24 (2.79)	1.77 (2.72)	7.20 (3.21)

Abbreviations: —, data not available; NS, nonsmokers; S, smokers.

^aValues converted to micrograms per liter assuming a mean urinary creatinine value of 11 mmol/L. ^bSubjects living in the vicinity of a creosote impregnation plant. ^cGSD not available.

^dMeasurements from postexposure samples in the low-exposure group.

respectively) were lower than levels observed in workers positioned at tops of coke ovens (58.5 and 34.1 $\mu\text{g/L}$, respectively; Serdar et al. 2003) but were comparable with those observed in working at the bottoms or sides of the same coke ovens (30.0 and 26.9 $\mu\text{g/L}$).

Because preexposure urine samples showed very little evidence of a trend from low to high JP-8 exposure (Table 2), we conclude that the urinary biomarkers of naphthalene are very short-lived. Previous studies suggested two-phase excretion kinetics for the naphthols in urine, consisting of a rapid phase with half-lives ($t_{1/2}$) of 1.2–4.6 hr, followed by a slower phase with $14 \leq t_{1/2} \leq 46$ hr (Bieniek 1994; Heikkilä et al. 1995). Our results suggest that most of the naphthols were eliminated during the rapid phase. Although the elimination kinetics of unmetabolized naphthalene have not been reported in urine, they probably track those of naphthalene in breath, which had an estimated $t_{1/2}$ of 22 min in our subjects (Egeghy et al. In press). Given such rapid removal, very little naphthalene would be expected on the day after exposure, consistent with our results.

In each exposure category, smokers had higher levels of urinary benzene, naphthalene, and the naphthols in both pre- and post-exposure samples. Because cigarette smoking is reportedly the greatest source of benzene among the general public (Ashley et al. 1996; Darrall et al. 1998), it is not surprising that smokers would have higher levels of urinary benzene than would nonsmokers. Among heavily exposed workers who did not smoke, levels of postexposure urinary benzene (GM = 1.81 $\mu\text{g/L}$) were about the same as values observed in low-exposed smokers (essentially control subjects; GM = 1.60 $\mu\text{g/L}$). This suggests that the contribution of benzene arising from JP-8 exposure in the heavily exposed subjects was roughly equal to that from cigarette smoking.

The postexposure levels of urinary benzene observed among our low-exposed subjects were somewhat higher than those reported among controls in other investigations (Table 6). On the other hand, postexposure measurements of urinary benzene from the high-exposure group (GM = 1.81 $\mu\text{g/L}$ for nonsmokers, 3.71 $\mu\text{g/L}$

for smokers) were comparable with those of workers in a shoe manufacturing plant (GM = 4.8 $\mu\text{g/L}$; Ong et al. 1995) and of workers in chemical plants and at gasoline pumps (GM = 1.26 $\mu\text{g/L}$ for nonsmokers, 2.6 $\mu\text{g/L}$ for smokers; Ghittori et al. 1993), but were much lower than the levels observed in workers heavily exposed to benzene as a solvent (GM = 50.2 $\mu\text{g/L}$; Waidyanatha et al. 2001).

Naphthalene is also present in cigarette smoke, albeit at lower concentrations than benzene (in mainstream smoke: naphthalene, 0.276 $\mu\text{g/cigarette}$; benzene, 39.8 $\mu\text{g/cigarette}$; Rustemeier et al. 2002). Thus, we anticipated that smokers would have somewhat higher levels of urinary naphthalene and the naphthols than nonsmokers. This was observed in all exposure categories (Table 3), consistent with previous results among Chinese coke oven workers and controls (Serdar et al. 2003; Waidyanatha et al. 2003). However, the effect of smoking upon naphthol levels was much less prominent than that of JP-8 exposure in our study; indeed, among heavily exposed subjects, the naphthols were not significantly greater in smokers than in nonsmokers but were about 10-fold greater than the corresponding levels in the low-exposure category (Table 3). Levels of urinary 1- and 2-naphthols in nonsmokers of the heavily exposed group (15.9 and 22.6 $\mu\text{g/L}$, respectively) were significantly higher than those of smokers in the low-exposure group (4.24 and 7.20 $\mu\text{g/L}$, respectively), suggesting that naphthalene exposure arising from JP-8 was more than three times higher than that from cigarette smoke.

If the exposures to surrogate compounds such as benzene and naphthalene originated from JP-8 among study subjects, it is reasonable to expect strong correlations among those surrogates in various biologic media, provided that the sampling times were sufficient for each analyte. We examined the relationships between levels of benzene and naphthalene in air, breath, and urine. Although significant correlation was generally observed between the naphthalene and benzene biomarkers in both pre- and postexposure samples, correlation coefficients observed for samples obtained after the work shift tended to be much larger (Tables 4

and 5). This supports the presumption that there was a common source of exposure to benzene and naphthalene during the work shift.

We conclude that JP-8 is a significant source of exposure to benzene and naphthalene. Among heavily exposed workers, JP-8 contributes about the same benzene dose as cigarette smoking and more than three times the naphthalene dose as cigarette smoking. Our results indicate that unmetabolized naphthalene, as well as 1- and 2-naphthol, could serve as possible short-term biomarkers of JP-8 exposure. Of these, the naphthols are probably more useful because of their greater abundance and slower elimination kinetics.

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