Environmental and Biological Monitoring of Benzene during Self-Service Automobile Refueling

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Although automobile refueling represents the major source of benzene exposure among the non-smoking public, few data are available regarding such exposures and the associated uptake of benzene. We repeatedly measured benzene exposure and uptake (via benzene in exhaled breath) among 39 self-service customers using self-administered monitoring, a technique rarely used to obtain measurements from the general public (130 sets of measurements were obtained). Benzene exposures averaged 2.9 mg/m³ (SD = 5.8 mg/m³; median duration = 3 min) with a range of 0.076–36 mg/m³, and postexposure breath levels averaged 160 µg/m³ (SD = 260 µg/m³) with a range of 3.2–1,400 µg/m³. Log-transformed exposures and breath levels were significantly correlated (r = 0.77, p < 0.0001). We used mixed-effects statistical models to gauge the relative influences of environmental and subject-specific factors on benzene exposure and breath levels and to investigate the importance of various covariates obtained by questionnaire. Model fitting yielded three significant predictors of benzene exposure, namely, fuel octane grade (p = 0.0011), duration of exposure (p = 0.0054), and season of the year (p = 0.032). Likewise, another model yielded three significant predictors of benzene concentration in breath, specifically, benzene exposure (p = 0.0001), pre-exposure breath concentration (p = 0.0008), and duration of exposure (p = 0.038). Variability in benzene concentrations was remarkable, with 95% of the estimated values falling within a 274-fold range, and was comprised entirely of the within-person component of variance (representing exposures of the same subject at different times of refueling). The corresponding range for benzene concentrations in breath was 41-fold and was comprised primarily of the within-person variance component (74% of the total variance). Our results indicate that environmental rather than interindividual differences are primarily responsible for benzene exposure and uptake during automobile refueling. The study also demonstrates that self-administered monitoring can be efficiently used to measure environmental exposures and biomarkers among the general public. Key words: benzene, biological monitoring, exhaled air, exposure, exposure variability, gasoline, mixed models, self-monitoring. Environ Health Perspect 108:1195–1202 (2000). [Online 15 November 2000] http://ehpnet1.niehs.nih.gov/docs/2000/108p1195-1202egeghy/abstract.html

Benzene is a volatile organic compound that is toxic to the hematopoietic system (1) and has caused acute myelogenous leukemia in populations with high-level occupational exposures (2,3). Although there is considerable doubt concerning the leukemogenic effect of benzene at lower concentrations (4,5), the suspicion that long-term exposure to even small amounts of benzene may be harmful (6–8), together with the widespread exposure of the general population (9–11), has caused concern.

Environmental concentrations of airborne benzene in the United States tend to range from 2 to 19 µg/m³, with the higher levels in urban areas (10). Because approximately 85% of atmospheric benzene is derived from mobile sources, higher concentrations are often found inside motor vehicles and adjacent to major roadways (8,12,13). Among nonsmokers the greatest short-term exposures to benzene arise from inhalation of gasoline vapors during automobile refueling. Although current regulations limit the benzene content of all grades of gasoline in the United States to 1% (v/v) (10,14), concentrations as high as 5% have been reported in Europe (15,16).

Self-service gasoline customers are exposed to benzene emitted from fuel combustion as well as from underground storage tanks, spills, and displacement of vapors from the fuel tank (17). Of these, displacement of fuel vapors is thought to be responsible for most of the exposure. A number of studies have found that exposures to benzene vary greatly during self-service refueling from a few parts per billion to several parts per million (18–21). Thus, the general population is regularly exposed to a known carcinogen, sometimes at high levels, albeit for short periods.

Following inhalation, benzene vapor is rapidly absorbed into the blood and distributed throughout the body (22,23). The kinetics of benzene uptake and distribution have been investigated among human volunteers under experimental conditions (24–30) and among occupationally exposed workers (31–41). These studies have relied on unmetabolized benzene in exhaled air (breath), blood, and urine, as well as benzene metabolites in urine. Of these, unmetabolized benzene in breath is an attractive measure of uptake because it is easily obtained by non-invasive means (42,43).

A few investigators have reported benzene uptake associated with gasoline refueling (44,45) and other ambient sources (46–49). In this study we report benzene exposures during self-service gasoline refueling and evaluate the relationship between benzene in ambient air and in breath. In doing so we will apply mixed-effects statistical models to evaluate effects related to the environment and to the individual person. Because such models require rather large sample sizes, we developed a self-administered test kit to assist subjects in obtaining measurements of benzene in ambient air and breath during refueling.

Materials and Methods

Sample collection. A test kit (Figure 1) was developed to facilitate measurements of benzene in air and breath without professional assistance. The kit contains a passive monitor for measuring personal exposure, two glass bulbs of 75-mL volume for obtaining breath (end-exhaled air), and simple illustrated instructions for their use. Both types of monitors are reusable.

The passive monitors consist of aluminum tubes (90 mm × 6.3 mm o.d. × 5.0 mm i.d.) fabricated to the dimensions of commercial stainless steel devices designed for this purpose. Each monitor contains 0.1 g of 20/35 mesh Tenax TA (SKC Inc., Eighty Four, PA). The adsorbent is maintained in place by stainless steel screens to create an open diffusion channel of 1.5 cm × 5.0 mm i.d. An additional screen, recessed 1 mm from the surface, serves as a turbulence barrier to maintain the stable concentration gradient.
necessary for constant diffusive uptake. Air sampling is initiated by simply removing one end cap from the monitor. This type of sampler has been used effectively for monitoring volatile organic compounds under various environmental conditions.

The locally fabricated breath samplers consist of glass bulbs (75-mL volume, 13-cm length) that are slightly larger than those used elsewhere for this purpose (43.51). The bulbs are sealed with threaded, plastic end caps containing PTFE-lined septa (Chemglass, Vineland, NJ). The subject is instructed to remove the end caps and then to completely exhale through the bulb. Because the bulb volume is small compared to the vital capacity, only end-exhaled air is collected. The subject can obtain the sample while located in a contaminated environment because any unabsorbed benzene from the anatomical dead space should be flushed from the bulb during the initial stage of exhalation. Significant losses are prevented by capping the free end of the device while it is still in the subject's mouth and then quickly replacing the remaining cap.

Subjects and conditions of measurement.

The study was conducted between July 1998 and March 1999, with samples collected during three different seasons (no measurements were taken during winter 1998/1999). Stage II vapor recovery controls were not used on gasoline pumps in the local area, but pump nozzles were outfitted with rubber splash collars. Pump nozzle latches were generally absent.

Although no qualifications were placed on participation, 27 of the 39 subjects were affiliated with the University of North Carolina. Thirty-four subjects were nonsmokers, three were smokers, and two did not indicate smoking status. Each subject was provided with two test kits at the time of recruitment and encouraged to obtain at least two independent measurements of exposure and breath levels; more kits were provided to subjects as needed. A total of 130 usable sets of measurements were obtained from 39 different participants, with 70% of the samples from males. Repeated measurements were obtained from 31 of the 39 participants. Subjects were instructed to obtain a preexposure breath sample while seated in their vehicle before refueling and then to immediately begin personal sampling by uncapping the passive monitor and clipping it to clothing in the breathing zone. After refueling, the cap was reattached to the passive monitor to terminate sampling, the postexposure breath sample was collected, and all times were recorded. No instructions were provided concerning the refueling process itself; participants were encouraged to refuel their vehicles as customary.

We provided a simple data sheet to assist subjects in recording the start and stop times for the environmental sampling as well as his or her height, weight, and sex. A variety of body types was represented in the study as summarized in Table 1. The questionnaire also requested information regarding several covariates related to the refueling process (i.e., duration, octane grade, time lag between refueling and postexposure breath sample, and general weather conditions).

About 5% of the kits were returned with poorly sealed breath monitors, and other types of user error invalidated three samples. These observations were excluded from the statistical analysis. Additionally, the process of concentrating the breath sample onto a thermal desorption cartridge failed in a few instances, and some measurements were lost due to instrument malfunction during analysis.

Preparation of monitors. Passive monitors were initially conditioned at 250°C for 30 min with a continuous flow of ultra high purity helium gas at a rate of 45 mL/min using an automatic thermal desorption system (Model ATD 400; Perkin-Elmer Corp., Norwalk, CT). Just before use, the monitors were also conditioned for 3 min at 250°C followed by 3 min at 225°C to remove trace levels of benzene. (Preliminary experiments determined that this two-step conditioning regimen produced lower levels of residual benzene than conditioning at a single temperature.) Breath sampling bulbs were thoroughly cleaned in an industrial glassware washer and the cap liners were replaced before each use.

Analysis of monitors. Before analysis, breath samples were transferred from the bulbs to air monitors using apparatus illustrated in Figure 2. Each septum was punctured with a 16-gauge needle, and the bulb was flushed with 400 mL zero-grade air at 100 mL/min through an air monitor (of the same type used for passive sampling) to capture the volatile constituents. To minimize surface and condensation losses, the bulb was heated to 90°C before this transfer.

Passive monitors and breath samples were initially analyzed with an Hewlett Packard 5890 Series II gas chromatograph equipped with a flame ionization detector (GC/FID), which was later replaced by an Hewlett Packard 6890 Series Plus GC/FID (Hewlett Packard Corp., Palo Alto, CA). Separation was achieved with a megabore DB-1, 60-m x 0.53-mm dimethylpolysiloxane column (1.5 μm film thickness; J & W Scientific, Folsom, CA). The oven temperature was held at 30°C for 13 min, increased at 50°C/min to a final temperature of 250°C, and held for 5 min. Ultra high purity helium was used as the carrier gas at a flow of approximately 8 mL/min. Chromatograms were manually integrated using an Hewlett Packard gas chromatography (GC) ChemStation software. Benzene was identified by the retention time of 10.97 min.

Samples were desorbed with a Perkin-Elmer ATD 400 automatic thermal desorption system (52.53) for 2 min at 225°C to...
transfer analytes onto a Tenax-packed, oxygen-free focusing cold trap maintained at -30°C. (Tenax is a registered trademark of Buchem B.V., Apeldoorn, Netherlands.) The cold trap was then rapidly heated to 225°C and held at that temperature for 0.1 min to transfer the contents to the analytical column via a fused silica transfer line, maintained at 200°C. No inlet or outlet splitting was used.

Samples were quantified against external standards by drawing precisely metered volumes of benzene vapor through identical adsorption tubes at 50 mL/min. All benzene vapor standards were prepared by serial dilution as follows: 2 µL liquid benzene (99.9%, Fisher Scientific, Pittsburgh, PA) was injected with a 10-µL syringe (Hamilton Co., Reno, NV) into a 250-mL sealed glass container from which various volumes were removed with a 250-µL Gastight syringe (Hamilton Co.) and injected into a 10- or 40-L Tedlar bag (SKC Inc.), which had been filled with a precisely metered volume of zero-grade air. For example, to achieve a benzene vapor standard of 0.035 mg/m³ (11 ppb), groups of at least 4 bulbs were analyzed after 0, 14, and 28 days had elapsed.

Statistical analysis. We used mixed-effects models to investigate levels of benzene in ambient air and breath using the MIXED procedure available with SAS Statistical Software (SAS Institute, Cary, NC). Histograms and the Shapiro-Wilk test for normality indicated that the distributions of exposure and breath concentration were positively skewed and approximately lognormal. These variables were log-transformed (base e) before analysis to provide nearly Gaussian distributions and to stabilize the variances. Two separate models were used: the first with the log-transformed benzene exposure as the response variable (Model 1), and the second with the log-transformed breath concentration as the response variable (Model 2).

The general mixed model equation is

\[ Y_{ij} = X_i \beta + Z_i \beta_i + e_i, \]

where \( Y_{ij} \) is a vector of observations of the response variable at different times for the \( i \)-th individual; \( X_i \) is a matrix of observed values of fixed-effect predictor variables for the \( i \)-th individual; \( A \) is a vector of fixed regression coefficients describing the association between \( Y \) and \( X_i \); \( Z_i \) is a matrix of observed values of random-effect predictor variables for the \( i \)-th individual; \( B \) is a vector of individual regression coefficients for these random effects; and \( e \) is a vector of within-person random errors.

Model 1 is presented in nonmatrix form as follows:

\[ Y_{ij} = \ln(X_{ij}) = \alpha_0 + \sum_{m=1}^p \alpha_m V_m + \beta + \varepsilon_i \]

for \( m = 1, 2, \ldots, p \) covariates,

\[ \text{for } i = 1, 2, \ldots, n_i \text{ individuals, } \]

\[ \text{for } j = 1, 2, \ldots, n_{ij} \text{ measurements of the } \]

\[ \text{the } i \)-th individual, \]

\[ \text{where } Y_{ij} \text{ represents the exposure level on the } \]

\[ \text{the } j \)-th day for the \( i \)-th individual, and } Y_{ij} \text{ is the } \]

\[ \text{natural logarithm of the individual measurement } \]

\[ X_{ij}. \]

The loged value \( Y_{ij} \) represents the sum of the effects consisting of \( \alpha_0 \) representing the intercept, \( \alpha_m \) representing the fixed effect for the \( m \)-th variable, \( \beta \) representing the random effect for the \( i \)-th individual, and \( \varepsilon_i \) representing the random error for the \( j \)-th observation on the \( i \)-th individual. Additionally, categorical variables were represented by g-1 indicator variables for the \( g \) levels of each variable. It is assumed that \( \beta \)s and \( \varepsilon_i \)s are normally distributed with means of zero and variances of \( \sigma^2_{\beta} \) and \( \sigma^2_{\varepsilon} \), respectively (representing the between- and within-person components of variance).

Figure 3. Apparatus for determining sampling rates of benzene by passive monitors. Passive monitors were exposed in duplicate to a well-mixed atmosphere with a benzene concentration of 3.2 mg/m³ (1.0 ppm) for short periods. Sampling rates (ng/ppm/min) were calculated from the mass of benzene absorbed (as determined by GC analysis) and the duration of the test.
The relationship between benzene in breath and benzene exposure is illustrated with the scatter plot shown in Figure 5. Because of the small intraclass correlation of exposure and breath measurements noted in Table 5, repeated measurements from the same individual can be treated as independent observations. Overall, we observed significant linear correlation between the 130 pairs of log-transformed exposures and breath levels ($r = 0.77, p < 0.0001$).

**Mixed-effects models.** Results of fitting Model 1 to the exposure data are summarized in Table 6. The final model contained three significant predictors of benzene exposure, namely, fuel octane grade ($p = 0.0011$), duration of exposure ($p = 0.0054$), and season ($p = 0.032$). Among the types of fuels, mid-grade unleaded gasoline was associated with the

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**Table 2.** CO$_2$ levels (%) in breath monitors.

| Subject | Sample 1 | Sample 2 | Sample 3 |
|---------|----------|----------|----------|
| A       | 4.7      | 4.7      | 5.1      |
| B       | 5.0      | NA       | 4.9      |
| C       | 4.1      | 4.4      | 4.2      |
| D       | 4.5      | 4.8      | NA       |
| E       | 5.1      | 3.4      | 3.6      |

NA, not available (lost during analysis). The weighted mean for all subjects is 4.56%.

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**Table 3.** Recovery (%) of benzene from breath monitors stored for various periods of time.

| Storage period | Mean recovery (%) | No. | SD | CV  |
|----------------|-------------------|-----|----|-----|
| No storage     | 100               | 4   | 1.3| 1.3 |
| 2 Weeks        | 96                | 4   | 1.5| 1.6 |
| 4 Weeks        | 92                | 5   | 6.0| 6.5 |

CV, coefficient of variation.

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**Table 4.** Summary of levels of benzene in environmental air and breath during automobile refueling.*

|          | No. | Mean ± SD (mg/m$^3$) | Minimum (mg/m$^3$) | Maximum (mg/m$^3$) |
|----------|-----|----------------------|---------------------|-------------------|
| Exposure | 130 | 2.9 ± 5.8            | < 0.076             | 36                |
| Breath, preexposure | 130 | 0.0086 ± 0.011 | < 0.0032             | 0.070            |
| Breath, postexposure | 130 | 0.16 ± 0.26         | < 0.0032             | 1.4              |

*Duration 1–10 min (median = 3 min).

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**Table 5.** REM-L estimates of covariance parameters based on mixed-effects models including important covariates.

| Measure                        | Variance component | Estimate | Percent of total | $R_{0.95}^*$ |
|-------------------------------|--------------------|----------|-----------------|-------------|
| ln(Exposure)                  | Between-person     | 0.00     | 100%            | 224         |
| ln(Exposure)                  | Within-person      | 0.05     | 100%            | 224         |
| ln(Exposure)                  | Between-person     | 2.05     | 100%            | 224         |
| ln(Exposure)                  | Within-person      | 0.23     | 26%             | 41          |
| ln(Exposure)                  | Between-person     | 0.67     | 74%             | 41          |

*$R_{0.95}$ fold range containing 95% of the lognormal distribution of levels.
highest benzene exposures and diesel fuel with the lowest; among seasons, fall was associated with the highest exposures and spring with the lowest. The magnitude of benzene exposure decreased with increasing duration. Figure 6 summarizes the effects of octane and season upon benzene exposure with duration held constant at the median value of 3 min. Neither the subject’s height nor any of the weather-related variables were found to significantly affect benzene exposure.

Fitting of Model 2 to the data yielded three significant predictors of benzene levels in breath, namely, benzene exposure (p = 0.0001), preexposure breath concentration (p = 0.0008), and duration of exposure (p = 0.038). Table 7 presents the parameter estimates for the model and the tests of fixed effects. The parameter estimate for duration of exposure was positive, in contrast to Model 1, where it was negative. None of the following variables were found to have a significant effect: time lag, sex, BMI, weight, or height.

**Discussion**

We observed remarkable variability of benzene exposures during automobile refueling, with 95% of the concentrations covering a 274-fold range (Table 5). Faced with such variability, our approach to increasing sample size was to use passive monitors suitable for use by the subjects themselves and to package the devices in simple test kits that can be transported via the mail. Although several recent studies have used self-monitoring to obtain exposure data from workers (61–63), we are unaware of any other application of self-monitoring to obtain exposure data from the general public.

Despite the simplicity of our study design and methods, the benzene exposures we measured were not markedly different from those reported in recent conventional studies of automobile refueling, as summarized in Table 8. We estimated a mean benzene exposure of 2.9 mg/m³ (n = 130), which compared to mean values of 1.3 mg/m³ (n = 120 measurements pooled from 1,013 self-service customers in the United States) (18), 0.9 mg/m³ (n = 59,600 exposures pooled from 167 self-service customers in Finland, where benzene is also limited to 1% by volume) (21), and a median value of 1.3 mg/m³ (n = 30 self-service customers in Alaska at temperatures of -3°C and below) (44).

Because we obtained repeated exposure measurements from the subjects, it was possible to estimate the within- and between-person variance components. Such partitioning of exposure variability allows inferences to be made regarding the relative influences upon exposure of both environmental factors, indicated by within-person variation, and subject-specific factors, indicated by between-person variation (64). That is, if exposure were governed largely by random factors related to the mix of locations, atmospheric conditions, content of benzene in fuel, duration of refueling, movements patterns, etc., experienced by a typical subject on different days, the within-person variance component would represent most of the variability. In contrast, if factors specific to the individual, such as body size, behavior (e.g., always fascineward from the nozzle during refueling), or type of vehicle were important, the between-person variance component would represent a sizable proportion of the total variation. Because the estimated within-person variance component (Table 5) accounted for all of the variation in benzene exposures estimated in our study, we conclude that environmental rather than subject-specific factors were primarily responsible for benzene exposures during automobile refueling.

In a study of benzene exposures among gasoline-station attendants, Lagorio et al. (65) similarly reported a large within-person component of variance, comprising about 83% of the total variance.

Our analysis yielded three significant predictors of benzene exposure, namely, fuel octane grade (p = 0.0011), season (p = 0.0322), and duration of refueling (0.0054). Regarding octane grade, benzene exposures were lowest when diesel fuel was dispensed and highest when mid-grade (89-octane) gasoline was dispensed. The finding that diesel fuel led to smaller exposures was expected because diesel fuel is known to have a very low benzene content, generally below 0.02% (66). However, the elevated exposures associated with mid-grade gasoline are more difficult to interpret. Octane grade does not refer to the hydrocarbon content but rather to the knock resistance of gasoline that can be achieved through a variety of

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**Table 6.** Fixed effects for benzene exposure.

| Effect          | Estimate | SE   | p-Value |
|-----------------|----------|------|---------|
| Intercept       | 0.25     | 0.39 | -       |
| Duration (min)  | -0.24    | 0.084| 0.0054  |
| Octane          | -        | -    | 0.0011  |
| Diesel          | -2.22    | 0.88 | 0.0131  |
| 87 Grade        | -0.04    | 0.30 | 0.0935  |
| 93 Grade        | 1.21     | 0.45 | 0.0001  |
| Season          | 0        | 0.00 | 0.0322  |
| Fall            | 0.27     | 0.35 | 0.4400  |
| Spring          | -0.53    | 0.30 | 0.0844  |
| Summer          | 0        | -    | -       |

**Table 7.** Fixed effects for benzene in breath after refueling.

| Effect          | Estimate | SE   | p-Value |
|-----------------|----------|------|---------|
| Intercept       | 3.05     | 0.217| 0.0001  |
| ln(Exposure)    | 0.70     | 0.051| 0.0008  |
| ln(Preexposure) | 0.32     | 0.091| 0.0008  |
| Duration (min)  | 0.11     | 0.055| 0.0384  |

**Table 8.** Recent short-term measurements of benzene concentration during gasoline refueling.

| Year | Reference | Country     | Avg duration (minutes) | No. | Mean (mg/m³) | Maximum (mg/m³) | % Benzene in fuel |
|------|-----------|-------------|------------------------|-----|--------------|-----------------|------------------|
| 1993 | Clayton et al. (18) | United States | 1.72 | 120a | 1.3 | 8.4 | 1.6a |
| 1997 | Backer et al. (44) | United States | 0.80 | 30b | 1.3 | 2.7 | 0.87 |
| 1999 | Vainio et al. (21) | Finland      | 1.13 | 8a  | 0.9 | NR  | 0.64 |

Abbreviations: Avg, average; No., not reported.

a Each sample was comprised of 8-10 (18) or 20-21 (21) different refuelings. b Range: 0.35-4.1. c Regular (non-ethanol) unleaded gasoline group only. d Median.
hydrocarbon blends (67), and no apparent association between octane grade and benzene exposure has been established. Only two recent studies provide data regarding the benzene content of different grades of gasoline. In the first of these, regular unleaded gasoline (87-octane) was reported to have the highest benzene content at four of six locations (18), whereas in the second, octane grade was reported to be inversely related to benzene content in two of three cities (68).

Regarding the seasonal effect on benzene exposure during refueling (\(p = 0.032\)), properties of the fuel (e.g., vapor pressure and benzene content) could be involved as well as meteorologic differences (17,19,37,65,69–73). Gasoline is often designated as either “winter blend” or “summer blend” because its volatility reaches a maximum during winter and a minimum during summer to ensure good “driveability” and to comply with regulations restricting evaporative hydrocarbon emissions (16,74). Previous studies have reported higher exposures in winter than in summer (20,75) and also have identified body orientation as an important contributor (in cold weather people tend to lean over the pump nozzle thereby placing their heads directly into the rising vapor stream) (20). Our finding that benzene exposures were higher in summer than in spring cannot readily be explained by known seasonal volatility differences in gasoline. Furthermore, our study included no winter measurements and thus did not permit the full range of seasonal factors to be investigated.

Duration of refueling was inversely related to benzene exposure in our investigation (\(p = 0.0054\)). Because Lagorio et al. (65) and Backer et al. (44) reported that the volume of fuel dispensed was an important predictor of benzene exposure among service-station attendants and self-service customers, respectively, our finding of lower exposures at longer durations of refueling might appear contradictory. However, given generally rapid gasoline dispensing rates (30–40 L/min) and the rather long refueling times in our study (ranging up to 10 min, with a median of 3 min), it seems unlikely that longer durations corresponded to larger dispensed volumes. Rather, we suspect that longer durations of refueling reflected ancillary tasks associated with payment, checking oil levels, cleaning windshield, etc., where benzene concentrations would be very low. Because individuals continued to wear the personal monitors during such periods of very low exposure, the time-weighted average air concentration recorded with a long duration (many ancillary tasks) would therefore be smaller than one with short duration (few ancillary tasks).

The mean concentration of benzene in breath before refueling was 8.6 µg/m\(^3\) (Table 4). Because benzene concentrations have been found to be 3–8 times higher inside a passenger vehicle than in ambient air (10,13,46), this level is probably higher than the background value in the ambient area. Background levels of benzene in the breath of nonsmokers have been reported to be between 0.8 and 5.3 µg/m\(^3\) in the United States (76) and to average 6.2 µg/m\(^3\) in an urban population in Sweden (77).

Immediately after refueling, benzene levels in the breath of our subjects ranged from <0.0032 to 36 µg/m\(^3\), with a mean value of 0.16 mg/m\(^3\). This range is consistent with a pair of measurements by Lindstrom and Piehl (45), who reported a benzene concentration of 0.025 mg/m\(^3\) for a single subject immediately after dispensing fuel and 0.007 mg/m\(^3\) for an observer. In a study of self-service gasoline refueling in Alaska, Backer et al. (44) reported benzene levels between 0.13 and 4.20 ppb in venous blood among 60 subjects. Assuming a blood/breath partition coefficient of 7.4 (38), these blood concentrations correspond to a range of benzene concentrations in alveolar air between 0.019 and 0.60 mg/m\(^3\), which also seems reasonable in light of our findings.

The range containing 95% of the postexposure breath concentrations was 41-fold compared to the 274-fold range for the corresponding distribution of exposures during refueling (Table 5). This reduction in variability of a biomarker (i.e., benzene in breath) relative to the corresponding exposure distribution arises from accumulation of the contaminant in the body and has been observed over both long and short time scales [reviewed by Rappaport (59)]. Such psychologic damping of exposure variability provides an impetus for using benzene in breath as a biomarker of exposure in future studies of automobile refueling.

Because three-fourths of the variability of benzene measurements in breath was associated with the within-subject variance component (Table 5), we conclude that breath levels were affected primarily by environmental factors operating at different times of refueling rather than by interindividual differences among the subjects. This conclusion is consistent with results shown in Table 7, which indicate that although benzene in breath (after refueling) was highly associated with both benzene exposure [\(\text{ln(Exposure)}\): estimated coefficient = 0.70, \(p = 0.0001\)] and the preexposure breath concentration [\(\text{ln(Preexposure)}\): estimated coefficient = 0.32, \(p = 0.0008\)], subject-specific differences in sex, height, weight, and BMI were not significantly associated with breath levels. The duration of exposure was also positively associated with benzene in breath (estimated coefficient = 0.11, \(p = 0.038\)) suggesting that over the few minutes our subjects were exposed, the benzene concentrations in blood and breath increased as the contaminant was distributed to the highly perfused tissues (43,78).

The ratio of the alveolar benzene concentration to inspired benzene concentration has typically been in the range of 0.4–0.6 at steady state [111–223 µg/m\(^3\) for 0.5–2 hr, Yu and Weisel (79); 80–100 µg/m\(^3\) for 3–4 hr, H unter and Blair (25)], whereas a medi- an value of 0.17 has been reported for mixed exhaled air among subjects exposed to benzene in residential settings (76). These ratios represent the fractions of the inhaled benzene dose that are exhaled unchanged at steady state (80). The median ratio of alveolar air to inspired air among our subjects was considerably lower at 0.06, again reflecting non-steady-state conditions associated with the short duration of exposure (43,78,81,82) and also reflecting the rapid elimination of benzene following exposure (82,83).

Likewise, we suspect that this brief duration of exposure reduced any potential effects of BMI and sex upon benzene in breath, which might have been anticipated due to variation in body fat among subjects (23,25). For example, previous chamber studies [80 mg/m\(^3\) for 2 hr, Sato et al. (29)] showed that women, who have more body fat than men, had decreased respiratory excretion of benzene compared to men, and physiologically based pharmacokinetic (PBPK) modeling [simulation of 32 mg/m\(^3\) for 8 hr, Brown et al., (84)] predicted that women would have greater metabolism of benzene than men.

Conclusions

This study documents exposure to benzene during self-service refueling. Using mixed-effects regression models and repeated measurements, we showed that the within-person component of variability was quite large for both exposures during refueling and the resulting concentrations in breath. This suggests that environmental rather than individual factors were primarily responsible for the magnitude of benzene exposure during refueling. Of the possible environmental factors affecting benzene exposure, we found significant effects due to fuel-octane grade (mid-grade gasoline produced the highest exposures), season (exposures were greatest in the fall), and duration of refueling (longer times led to lower air concentrations). We also found that levels of benzene in breath were greatly affected by the exposure concentration and the preexposure breath level of benzene, and that the duration of refueling increased breath levels slightly. Finally, this study demonstrated the utility of self-collection of samples of both environmental air and breath among subjects from the general...
population. Although not yet in common practice, self-administered monitoring offers an efficient alternative to traditional methods for collecting the large numbers of measurements necessary to accurately characterize exposures and the relationships between exposure and biomarker levels.

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