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A field method for measuring solvent vapors in exhaled air — application to styrene exposure

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RAPPAPORT SM, KURE E, PETREAS M, TING D, WOODLEE J. A field method for measuring solvent vapors in exhaled air — application to styrene exposure. Scand J Work Environ Health 1991: 17:195—204. A method is described for measuring solvent vapors in mixed-exhaled air. The subject exhales through a carbon-containing tube connected to a Wright respirometer. Adsorbed vapors are subsequently eluted by carbon disulfide and analyzed by gas chromatography. Twenty-minute exposures to styrene and the corresponding concentration of styrene in the breath and venous blood were repeatedly measured for two subjects. Regression analyses indicated that the breath measurements were highly correlated with both the exposures and the blood concentrations of styrene. In another study, styrene was measured simultaneously in the mixed-exhaled air by this technique and in the end-exhaled air by a portable gas chromatograph. The mixed-exhaled air obtained with this method contained about half alveolar air. Analysis of the components of the variance obtained from all the data indicated that the error in measurement by this method was about one-fourth of the total variance.

Key terms: alveolar air, blood, breath, carbon adsorption, end-exhaled air, mixed-exhaled air, solvent vapors.

Biological monitoring of workers exposed to organic solvents is desirable because it allows the uptake of the substances to be estimated regardless of the route of exposure. Of the currently used techniques, measurement of the vapor in exhaled air is particularly attractive because it is noninvasive. [See recent reviews by Droz & Guillemin (1) and Wilson (2)]. Breath sampling in field studies has relied upon the collection of mixed- or end-exhaled air in either glass tubes (eg, references 3 and 4) or in bags made of inert polymers or metal foils (eg, reference 5). After the collection of exhaled air, the analyte can be measured directly in the field if a suitable instrument (eg, that presented in reference 6) or analytical method (5) is available. However, the receptacle containing the analyte is generally transported to a laboratory for analysis. In some cases, the analyte is preconcentrated from the sampling device by the withdrawing of air from the receptacle through an appropriate sorbent (as, eg, in references 7 and 8).

In contemplating a large field investigation of styrene exposure in the reinforced plastics industry, we evaluated several of the existing techniques for measuring styrene vapor in exhaled air and found them unsuitable for two reasons. First, we required a technique which would allow between 100 and 200 breath samples to be gathered in a single day. This necessity made it impractical to collect breath in bags or other bulky containers or to preconcentrate styrene from such receptacles. Second, we required a method which would allow samples to be easily transported and stored for several days prior to analysis. Our experience with laboratory trials indicated that styrene vapor was absorbed by even “inert” polymers such as Teflon and was irreversibly lost in glass containers if not analyzed within hours of collection.

In seeking an alternative field procedure, we were intrigued by the description of a method in which solvent vapor was concentrated directly from the breath as the subject exhaled through a tube containing activated coconut carbon (personal communication, 1986, J Fajen, National Institute for Occupational Safety and Health, Cincinnati, Ohio, United States). Since coconut carbon is used routinely for the air monitoring of styrene and other organic solvents in the workplace (9), and because styrene vapor has been shown to be stable following adsorption by coconut carbon (10), we thought that such a technique would be amenable to the collection of large numbers of samples and would allow samples to be stored for several days prior to analysis. In what follows we report the application of this technique to measure styrene repeatedly in mixed-exhaled air obtained from two subjects in the workplace. Preliminary results are also presented from a larger investigation in which mixed-exhaled air and end-exhaled air were measured simultaneously for 27 workers who were exposed to styrene.

The studies were designed to determine whether coconut carbon could be used in the field to determine the levels of styrene in the breath accurately. If this were the case, we expected to observe that the exhaled air concentration obtained by this technique would be proportional to the concentration of styrene measured...
simultaneously in venous blood and in end-exhaled (alveolar) air. We also anticipated that, because styrene is rapidly cleared from the blood (11), the concentration of styrene in exhaled air would be related to the corresponding exposure during the 20 min or so preceding the breath measurement.

**Subjects and methods**

**Experimental design**

Two studies were performed. In the first, serial samples of environmental air, exhaled air, and blood were collected from two subjects in a factory where styrene was used in the manufacture of reinforced fiber glass products (bathtubs and showers). The subjects were exposed to styrene for 4 h as they observed the work practices of employees engaged with spraying styrene-containing resins into molds and laminating the products by hand. The factory was naturally ventilated with air supplied through large doors and other openings. On the day of the investigation, the ambient temperature was very warm, about 40°C. The subjects' exposures to styrene were measured at intervals of about 20 min with the use of pumps and carbon tubes. Mixed-exhaled air samples were collected in an area free of styrene to ensure that the analyte had been released from the blood and was not merely unabsorbed styrene from the anatomic dead space. Thus at the end of each exposure the subjects exited the workplace to an outdoor location where the ambient concentration of styrene was negligible. There, the blood and breath samples were collected and the carbon tubes were changed for the next determination. The mean interval that the subjects were absent from the workplace between exposures was 3.8 (SD 1.3) min. After 4 h of exposure, additional samples of blood and breath were obtained at 20-min intervals for 2—3 h so that the elimination rate of styrene could be determined. During this period the subjects were more-or-less sedentary.

The second study was designed to determine the relationship between the concentration of styrene in the mixed-exhaled air, as measured with the new method, and the concentration of styrene in the end-exhaled air (alveolar air), measured with a portable gas chromatograph. Samples were obtained from 27 workers who were employed in a factory where fiber glass boats were manufactured. The subjects were taken to an area free of styrene where mixed- and end-exhaled air samples were obtained within a few seconds of each other.

**Subjects**

In the first study, two healthy subjects volunteered with informed consent to participate. One subject was male, 29 years of age, and 170 cm tall, and weighed 63.9 kg (16% fat). The other subject was female, 26 years of age, and 152 cm tall, and weighed 52.0 kg (16% fat). Neither subject had been significantly exposed to styrene in the month preceding the investigation. In the second study, samples of mixed- and end-exhaled air were obtained with informed consent from 27 workers of both sexes who were exposed routinely to styrene.

**Styrene in environmental air**

The subjects' exposures to styrene were measured by personal monitoring with battery-operated pumps and tubes containing 150 mg of coconut carbon (number 226-35, lot 120, SKC West, Fullerton, California, United States). The airflow rate was 0.6 l/min. After the collection, the carbon tubes were sealed with polyethylene caps and stored at 4°C in an area free of styrene. Thirteen days after the collection, the carbon sections (100 mg primary section, 50 mg backup section) were removed from the tubes and placed in 4-ml glass vials. Three milliliters of carbon disulfide (Omnisolve, liquid chromatographic grade) was added to the carbon, and the vials were capped with Teflon-lined rubber septa. After 1 h of gentle agitation at room temperature, the solutions were analyzed by gas chromatography. One-microliter aliquots of the solutions were injected into a Varian model 3700 gas chromatograph equipped with a flame ionization detector. The glass column was 2 mm (inner diameter) × 2 m, packed with 10% SP-2100 on 80/100 Supelcoport (Supelco, Bellefonte, Pennsylvania, United States). The carrier gas was nitrogen at a flow rate of 38 ml/min. The column, injector, and detector temperatures were 95°, 210°, and 240°C, respectively. The peak areas of the samples were measured with a Varian Vista 401 data system and compared against those obtained from analytical standards prepared by the injection of known amounts of styrene (Aldrich, 99% + Gold Label) into carbon disulfide. The samples were corrected for the desorption efficiency of styrene from carbon, as will be described. The analysis of the backup sections of the carbon tubes indicated that there was no breakthrough of styrene.

**Styrene in blood**

Blood was collected from the subjects through an indwelling catheter inserted into the brachial vein at the beginning of the experiment. At the end of each exposure between 8 and 10 ml of blood was obtained in heparinized containers. Approximately 1 h after the cessation of exposure, blood was transferred to tared glass vials (20-ml capacity). One milliliter of hexane containing 8.86 µg/ml of chlorobenzene (internal standard) was added, and the vials were sealed with Teflon-lined caps, shaken vigorously and immediately frozen in dry ice. The samples were maintained at −20°C for 14 d prior to the analysis.

The analytical method was adopted from Karbowsk & Braun (12). After thawing, the samples were weighed and centrifuged. The hexane layer was transferred to a 4-ml glass vial with a Teflon-lined septum whereupon
Collection of samples. Prior to the collection of a sample, the ends of the glass tube containing the carbon were broken with a special tool and smoothed with a piece of carborundum. Then the tube was inserted into the apparatus and a disposable mouthpiece was affixed to the inlet. It was the most convenient for the subject and the investigator to sit facing each other across a small table. During the collection of the sample, the subject was instructed to maintain a comfortable but constant pressure as he or she exhaled through the device. This situation was easily accomplished by allowing the subject to observe the pressure reading on the gauge as the sample was obtained. A total of 3.0 l (uncorrected) was obtained for each sample in 0.5-l increments. The subject was coached to take a breath and then to exhale through the device until instructed to

Styrene in mixed-exhaled air

Apparatus. Exhaled air samples were obtained with the apparatus illustrated in figure 1. The subject forcibly exhaled through a disposable mouthpiece (cardboard number 1021—250, Vacumed, Inc, Ventura, California, United States) which was connected to a 1-cm (outer diameter) x 8.5-cm glass tube containing 200 mg of 20/40 mesh coconut carbon (tubes were obtained as a special order from SKC West and contained lot number 120 carbon). The outlet from the carbon tube was connected to a Wright respirometer (Haloscale 00—301, Ferraris Development and Engineering Ltd, London), which measured the volume of air passing through the apparatus. Connections between the carbon tube and the mouthpiece and the respirometer were made with special parts machined from aluminum and connected by Swagelok (1.0-cm inner diameter) brass fittings and Teflon ferrules. A small port in the upstream fitting was connected with plastic tubing to a pressure gauge [Magnahelic model 2203, Dwyer Instruments, Inc, Michigan City, Indiana, United States; 0—155 mm Hg (0—144 Pa)].

Correction of air volume. The resistance to exhalation imposed by the carbon tube reduced the volumetric flow rate through the Wright respirometer below the linear range of operation. However, we found that by monitoring and recording the pressure upstream from the carbon tube during exhalation, we were able to correct the volume since the observed and true volumes were found to be proportional at a given pressure. Before and after each field experiment, we calibrated the apparatus by connecting the inlet to a source of compressed air and the outlet to a dry gas meter. The air pressure was then increased in small increments over the working range of 21 to 72 mm Hg (19.2—67.0 Pa); at each pressure, the observed and true volumes which passed through the respirometer were noted. A typical calibration curve is shown in figure 2. We corrected the volumes by dividing the measured volume by the correction factor, which was the ratio of the observed to the true air volume obtained from calibration.
stop by the investigator, who monitored the volume recorded by the respirometer. In practice about 5—10 s were required for each 0.5-l exhalation. The subject repeated the process until six exhalations had been performed. The final volume and the pressure maintained during the collection of the sample were recorded by the investigator. The tubes were sealed with polyethylene caps and stored in an area free of styrene prior to the analysis.

Analysis of samples. The samples were analyzed 12 d after the collection. Carbon was removed from the tubes, desorbed with 1.5 ml of carbon disulfide, and analyzed by gas chromatography as described for the environmental air samples. The samples were corrected for the desorption of styrene from the carbon as will be described. The quantitation limit was estimated to be 0.8 μg of styrene per sample (0.4 μg styrene/100 mg carbon), or about 0.2 μg/l in an air sample with a corrected volume of 4 l.

Styrene in end-exhaled air
A portable gas chromatograph (Photovac Instruments, Ontario, Canada, model 10550) was modified to allow styrene to be measured in end-exhaled air. This instrument was equipped with a photoionization detector operated at an ionization potential of 11 eV. The analytical column (10 m x 0.53 mm (inner diameter), DB-5, 1.2 μm film thickness (Alltech Associates, Deerfield, Illinois, United States)) was operated at 40°C. The carrier gas was air at a flow rate of 20 ml/min. The inlet of the instrument was connected to a Haldane-Priestley tube (described by Wilson in reference 2) consisting of a coiled piece of stainless steel tubing of 83 x 0.75 (inner diameter) cm and fitted with a disposable mouthpiece (cardboard number 1021—250, Vacumed Inc) at one end. The instrument was calibrated in the laboratory by the preparation of standards in Tedlar bags (SKC West), from which samples were drawn directly into the gas sampling valve. The working range was 4 to 220 μg/l. The instrument was calibrated in the field against a 10-ppm standard of styrene in nitrogen (Scott Specialty Gases, Plumsteadville, Pennsylvania, United States).

A pressure gauge (Magnahelic gauge, 0—100 mm Hg (0—96 Pa), Dwyer Instruments, Michigan City, Indiana, United States) monitored the pressure at the inlet of the Haldane-Priestley tube as the subject exhaled through the device. At the end of the exhalation, which was signaled by a drop in pressure, 1 ml of air was drawn from the center of the Haldane-Priestley tube into the sampling loop of the gas chromatograph.

The gas chromatograph, as received from the manufacturer, had a significant memory for styrene which carried over between injections. This memory was traced to the absorption of styrene in the inlet and transfer lines, which were constructed of Teflon tubing, and to a Teflon switching valve which was an integral part of the instrument. By replacing the tubes with stainless steel, we were able to reduce the memory to about 15 % of the value from the previous injection. The sample concentrations were adjusted for residual styrene by injecting clean air (room air drawn through 1.2 g of 20/40 mesh activated coconut carbon) between samples so that the background levels could be determined. The precision of the method was estimated to be between 5 and 10 % as a coefficient of variation (six determinations with between four and six measurements/determination). The quantitation limit of the method was 1.7 μg/l.

Determination of desorption efficiency
Addition of solutions containing styrene. Known quantities of styrene (2—300 μg) were added in triplicate to 200 mg portions of SKC carbon (Lot 120, SKC West) in sealed 4-ml glass vials. The styrene was administered in 5 μl of carbon disulfide, and the vials were capped with Teflon-lined septa. After 20 h the carbon was desorbed and analyzed by gas chromatography as has already been described.

Collection of styrene vapor. Groups of three exhaled air tubes were exposed to styrene atmospheres produced dynamically. Air was generated at a flow rate of 30 l/min and at 50 % relative humidity and 25°C by a special system (model HCS 202, Miller Nelson Research, Carmel Valley, California, United States). Liquid styrene was injected continuously into the air stream by a syringe pump (Sage Instrument Co, model 355, Cambridge, Massachusetts, United States), containing either a 10- or 100-μl syringe, the needle of which had been inserted through a septum into the air stream. The vapor-air mixture entered a Teflon chamber (3.2 cm (inner diameter) x 76 cm) from which samples of the atmosphere were withdrawn through ports arranged radially 25 cm from the exit. The carbon tubes were connected to the ports with minimal lengths of Teflon tubing. The airflow rate through the tubes was maintained at 0.17 l/min with critical orifices. Five groups of samples were collected at styrene concentrations of either 4 or 25 μg/l for periods ranging between 5 and 42 min. After the collection, the samples were immediately desorbed with carbon disulfide and analyzed by gas chromatography as has already been described.

Results and discussion
Desorption efficiency
At low loadings of styrene on the coconut carbon (<30 μg/100 mg carbon) we observed that relatively large amounts of the adsorbate were not released by carbon disulfide. Thus, while only minor corrections for recovery were required for samples of environmental air
Styrene in air, breath and blood

The results of measurements of serial exposures to styrene for two subjects and the corresponding concentrations of styrene in the mixed-exhaled air and in the blood are shown in figure 4. It is apparent that the breath concentrations measured with the new technique were closely related to the concentrations of styrene in blood samples collected at the same time. The figure also shows that the concentrations of styrene in both the blood and the breath reflected the exposure received during the preceding 20 min.

When the mixed-exhaled air concentrations (MIXED) obtained from each subject were regressed first upon the blood concentrations (BLOOD) and then separately upon the preceding exposures (EXPOSURE), as shown in figure 5, the relationships revealed

\[
\text{Corrected amount (\text{\(\mu\)g}) = (C)(V) + (X)(weight carbon, mg)/100,}
\]

where X was determined from the above relationship. Corrections based upon the vapor-spiking data, where \(X=0.801(C^{0.706})\), would have yielded corrected amounts of styrene which were 1.9—8.8 % larger over the range of concentrations (values of C) between 0.3 and 300 \(\mu\)g/ml.

Figure 3. Results of the desorption of styrene from coconut carbon with carbon disulfide. The data were linearized to the Freundlich isotherm, according to the method described by Rudling (13). The x-axis is the liquid concentration of styrene \([C (\mu\text{g}/\text{ml})]\), and the y-axis is the residual amount of styrene adsorbed by the carbon \([X (\mu\text{g}/100 \text{ mg carbon})]\). [Note: \(X = V (C_0 - C)(100/\text{weight carbon, mg})\), where \(V\) is the volume of carbon disulfide and \(C_0\) is the hypothetical liquid concentration with the assumption of no adsorption]. Figure 3 indicates that, because the fit of the data to the isotherm was good, the underlying relationship can be used to correct samples for recovery. The figure also shows that the desorption behavior of the carbon was very similar regardless of the method by which styrene was added (either from liquid solution or from collection of the vapor), particularly in the range of \(C = 1—20 \mu\text{g/ml}\) where the corrections are the greatest. The least-squares regression obtained from the more extensive and accurate set of data (addition of liquid solutions) yielded the relationship \(X = 0.758(C^{0.522})\). The correction for desorption was easily applied as:

\[
\text{Corrected amount (\text{\(\mu\)g}) = (C)(V) + (X)(weight carbon, mg)/100,}
\]

where X was determined from the above relationship. Corrections based upon the vapor-spiking data, where \(X=0.801(C^{0.706})\), would have yielded corrected amounts of styrene which were 1.9—8.8 % larger over the range of concentrations (values of C) between 0.3 and 300 \(\mu\)g/ml.

### Figure 4

Figure 4. Results of serial measurements of exposure to styrene (Air), of styrene in the venous blood (Blood), and of styrene in the mixed-exhaled air (Breath) from two subjects in a factory where reinforced plastics were manufactured. (Conc = concentration)
strong linear correlations between the variables (table 1). Analysis of the residual errors from the regressions showed no evidence of nonlinearity and indicated that the residuals were normally distributed with constant variances over the ranges of BLOOD and EXPOSURE which were encountered. Since none of the intercepts from the simple regressions shown in table 1 were significant, we repeated analyses by forcing the regressions through the origins. Then the slopes, obtained from the two data sets, were averaged to yield the following relationships:

\[
\text{MIXED} = 4.86 \times 10^{-3} (\text{BLOOD}) \quad (SE = 1.17 \times 10^{-2}; N = 2),
\]

(eq 1)

Figure 5. Linear regressions of styrene in mixed-exhaled air of two subjects on styrene in venous blood and on exposure to styrene. The data are depicted in figure 4 and the results of the regression analyses are given in table 1. (Conc = concentration, \(r^2\) = correlation coefficient)

Table 1. Results of the linear regression of styrene in mixed-exhaled air (MIXED) on styrene in blood (BLOOD) and on exposure to styrene during the preceding 20 min (EXPOSURE), all expressed in micrograms of styrene per liter. (N = the number of measurements, \(\beta_0\) = the intercept, \(\beta_1\) = the slope, and \(r\) = the sample correlation coefficient)

|          | N  | \(\beta_0\) | \(\beta_1 (\times 10^3)\) | \(r^2\) |
|----------|----|-------------|--------------------------|--------|
| Subject 1 |    |             |                          |        |
| BLOOD    | 19 | 0.035\(^\dagger\) | 5.91***                 | 0.798  |
| EXPOSURE | 12 | 0.549\(^\dagger\) | 11.0***                 | 0.665  |
| Subject 2 |    |             |                          |        |
| BLOOD    | 17 | -0.137\(^\dagger\) | 4.06***                 | 0.734  |
| EXPOSURE | 12 | -0.025\(^\dagger\) | 11.2***                 | 0.844  |

\(^\dagger\) P \(\geq\) 0.13, *** P < 0.001.
and

$$\text{MIXED} = 1.27 \times 10^{-2} \text{ (EXPOSURE)} \ (SE = 0.17 \times 10^{-2}; N = 2),$$

(eq 2)

where the units of the three variables are all equivalent. Although these equations were based upon data obtained from only two subjects, and should therefore be considered as preliminary, they are used to explore other relationships in subsequent sections of this paper.

**Elimination of styrene in breath**

During the 2—3 h immediately following exposure to styrene, the concentrations of vapor in the breath should be governed by first-order kinetics with a decay curve which is dominated by the release of styrene from a large central compartment (11). In figure 6 the logarithms of the concentrations of styrene in the mixed-exhaled air were plotted against time after exposure. In both cases, the fit of the data to the single-compartment model was good with $r^2 = 0.90$ for sub-

![Figure 6: Decay curves of styrene in the mixed-exhaled air of two subjects after 4 h of exposure. The first order rate constants were 0.643 h$^{-1}$ (subject 1) and 0.643 h$^{-1}$ (subject 2). The data are shown in figure 4. (Conc = concentration, $r^2$ = correlation coefficient)](image)

**Figure 7. Regressions of styrene in the mixed-exhaled air of 27 workers on styrene in the end-exhaled air measured at the same time. (A = regression of the raw data, B = regression of the natural logarithms of the data, $r^2$ = correlation coefficient)**

![Figure 7](image)
ject 1 and \( r^2 = 0.87 \) for subject 2. The slopes of the two curves were \(-0.643 \, \text{h}^{-1} (SE = 0.089) \) for subject 1 and \(-1.097 \, \text{h}^{-1} (SE = 0.187) \) for subject 2; these values correspond to elimination half-times of 1.1 h (subject 1) and 0.63 h (subject 2). These half-times are consistent with the value of 0.584 h reported by Ramsey et al (11) for the central compartment of a two-compartment open model which had been fitted to breath concentrations observed for four subjects exposed to 80 ppm of styrene for 6 h.

**Mixed- versus end-exhaled air**

It is generally assumed that the mixed-exhaled air of a subject breathing normally is comprised of 70% alveolar air and 30% inhaled air (14). Since the method of breath collection described in this report imposes a restriction on normal breathing which results in a protracted exhalation of fixed volume (0.5 l uncorrected for pressure), we wished to determine empirically the proportion of the mixed-exhaled air which was alveolar. Thus we investigated pairs of samples of mixed and end-exhaled air which had been collected from 27 workers exposed to styrene.

A simple linear regression of mixed-exhaled air on end-exhaled air (END), shown in figure 7 A, yielded the relationship \( \text{MIXED} = -0.334 + 0.828(\text{END}) \), \( r^2 = 0.83 \). However, an analysis of the residual errors indicated nonlinearity and nonconstant variance across the range of the end-exhaled air concentrations. When the natural logarithms were taken of MIXED and END, the residual errors, from the analogous regression, indicated no lack of linearity and a constant variance. A plot of the log-transformed data is depicted in figure 7 B. After removal of the point at (1.026, -1.347), the residual of which was detected as an outlier (0.01 < \( P < 0.05 \)) (15), this model yielded the following relationship:

\[
\text{MIXED} = 0.470(\text{END})^{0.345} \quad (r^2 = 0.86; \ N = 26), \quad \text{eq} \ 3
\]

where both the intercept and slope were highly significant (\( P < 0.0001 \)).

The model defined by equation 3 indicates that the ratio of mixed-exhaled air to alveolar air varied over the experimental range. On the assumption that most individuals working with styrene-containing resins would be exposed in the range of 5—50 ppm of styrene (21.3—213 mg/m\(^3\)) then, from equation 2, the anticipated concentrations of mixed-exhaled air would be 0.270 mg/m\(^3\) < MIXED < 2.70 mg/m\(^3\), and from equation 3 the corresponding ratios would be 0.422 < MIXED/END < 0.660. Thus it appears that the concentration of mixed-exhaled air, as measured with this method, should typically be about half of that of the alveolar air.

**Partitioning the variability of breath measurements**

The presented data indicate that the variability of the breath concentrations of styrene was relatively large. For a better perspective of the results, it is necessary to partition the total variation into several parts. This partitioning can be accomplished with an analysis-of-variance model in which it is assumed that there are three major components of variability, those associated with changes in breath concentration within individuals over time, those associated with consistent differences between individuals, and those associated with errors in measurement. If it is assumed that each of these sources of variability is lognormally distributed, then the total variation can be accounted for conveniently as follows (16):

\[
s_1 = s_2L,T + s_2L,B + s_2L,M,
\]

where \( s_2L,T \), \( s_2L,B \), and \( s_2L,M \) represent the estimated variances of log-transformed data for the total distribution, the intra- and interindividual distributions, and the distribution of measurement errors, respectively.

The presented data allow the three components of the total variance to be estimated. The error in measurement can be estimated from the data regarding the elimination of styrene in the breath, shown in figure 6, if it is assumed that the residual error arises entirely from the collection and analysis of breath samples. Since the decay curves fit the single-compartment model well, and in light of earlier results by Ramsey et al (11), this assumption seems reasonable. Thus \( s_2L,M \) should be equivalent to the residual mean-square error from the analyses of variance of ln(conc) versus time, which was \( s_2L,M = 0.050 \) for subject 1, over the range of 0.43—3.1 \( \mu \text{g/l} \) (\( N = 8 \)), and \( s_2L,M = 0.139 \) for subject 2, over the range of 0.31—2.4 \( \mu \text{g/l} \) (\( N = 7 \)). These values can be pooled to yield a single estimate of \( s_2L,M = 0.091 \).

The estimated intrиндивидуal variance can be derived from the serial breath measurements obtained from two subjects (figure 4), since the variance of these data represents the sum of \( s_2L,W + s_2L,M \). Taking logarithms of the data and estimating sample variances, we obtained values of \( [s_2L,W + s_2L,M] = 0.221 \) and 0.252 for subjects 1 and 2, respectively. These values can also be pooled to yield a single estimate of \( [s_2L,W + s_2L,M] = 0.236 \). Subtracting the measurement error of \( s_2L,M = 0.091 \), we obtained the value of \( s_2L,W = 0.145 \). Since the intrиндивидуal variance reflects the variation in exposure which occurs over short periods, it is likely that different workplaces and jobs will result in different variances (17). Thus the estimate of \( s_2L,W = 0.145 \) should only be considered representative of continuous exposure in a naturally-ventilated workplace. Fortunately, much of the heaviest exposure to styrene occurs in the manufacture of reinforced plastics in such workplaces; therefore it seems appropriate...
to use this value to represent the intraindividual variance in the model.

The interindividual variance can be estimated from the regression of \( \ln(\text{MIXED}) \) on \( \ln(\text{END}) \) shown in figure 7B if it is assumed that the residual error arises from measurement error and from consistent differences in the exhalation of styrene between people. In this case the residual error is equivalent to \( [s_{L,B}^2 + s_{L,M}^2] = 0.195 \). Therefore, by subtracting the error in measurement of \( s_{L,M}^2 = 0.091 \), we obtained a value of \( s_{L,B}^2 = 0.104 \). Finally, by taking the sum of the three components, we estimated the total variance to be \( s_{L,T}^2 = 0.091 + 0.146 + 0.104 = 0.340 \). The individual variances can now be expressed as proportions of the total, where \( s_{L,M}^2/s_{L,T}^2 = 0.266 \), \( s_{L,W}^2/s_{L,T}^2 = 0.428 \), and \( s_{L,B}^2/s_{L,T}^2 = 0.305 \). Thus the error of measurement should contribute only about one-fourth of the total variance observed in the breath samples when \( s_{L,W}^2 \) reflects the variability in breath measurements within individuals, which is associated with short-term variation in exposure. If this method were applied to breath concentrations at the beginning of work, following 16 h of nonexposure, then \( s_{L,W}^2 \) would result from the presumably smaller variation in exposure which occurs over longer periods (1). Then \( s_{L,W}^2 \) would contribute between about one-fourth and one-half of the total variance.

Concluding remarks

The method described in this paper for the measurement of mixed-exhaled air should be suitable for predicting either the uptake of or exposure to styrene over the ranges of concentrations typically encountered in the workplace. This conjecture is supported by a longitudinal study of 48 styrene-exposed workers in which mixed-exhaled air measurements were found to be significantly correlated with long-term exposure and with sister chromatid exchanges in peripheral lymphocytes (18).

The precision of this method, estimated by \( s_{L,M}^2 = 0.091 \), represents the combined random errors from all sources related to the collection and analysis of the samples, including use of the Wright respirometer in the field and desorption of the carbon and gas chromatography. The precision can also be given in terms of the coefficient of variation (CV) by employing the relationship \( CV = [\exp(s_{L,M}^2 - 1)]^{0.5} = 0.31 \). Although a coefficient of variation of 31 % is relatively large when compared with that associated with the measurement of styrene in a single sample of environmental air (5.8 %) (9), it should be repeated that this error contributed no more than one-fourth of the total variability in the field measurements. The other three-fourths of the total variability arose from factors which were not related to the methodology but rather to temporal changes in exposure and to differences between individuals. Since these latter variables ultimately dominate the behavior of a breath monitoring program, it is clear that many measurements are required before occupational exposures can be assessed properly. Thus it can be seen that the real utility of a simple field monitor such as the one described in this paper lies not in its precision, but rather in its convenience and low cost.

Although the application described in this paper involved exposure to styrene, it should be clear that this method for measuring concentrations of vapor in the breath can easily be extended to other organic solvents which are stable on activated carbon. We have recently applied this methodology to workers exposed to tetrachloroethylene in the dry-cleaning industry (unpublished data).

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