Bull. Environ. Contam. Toxicol. (1986) 36:364–371

Bulletin of Environmental Contamination and Toxicology

Environmentally Significant Volatile Organic Pollutants in Human Blood

Shelley R. Antoine,[1] Ildefonso R. DeLeon,[1] and Roberta M. O'Dell-Smith[2]

[1]Center for Bio-Organic Studies, University of New Orleans, New Orleans, LA 70148 and [2]Department of Biological Sciences, University of New Orleans, New Orleans, LA 70148

Volatile organic compounds are an important category of commercial and industrial chemicals whose common and frequent usage has rendered them ubiquitous in the environment. Included in this class are many toxic volatile aromatic and halogenated organics. The occurrence of these chemicals as environmental pollutants, as well as their potentially toxic nature, has prompted numerous studies aimed at determining their presence and impact on the environment and on human health. Our own laboratory has previously examined drinking water sources (Dowty et al. 1975a, Dowty and Laseter 1975, Dowty et al. 1976a, Dowty et al. 1979) for volatile organic pollutants, and has attempted to correlate their occurrence to the presence of the same chemicals in human blood plasma (Dowty et al. 1975a, Laseter and Dowty 1977). In related studies, this laboratory has compared volatile organics in blood plasma before and after dialysis (Dowty et al. 1975b), and has presented evidence for the transplacental migration of certain volatile organics in paired cord blood and maternal blood (Dowty et al. 1976b).

As part of our continuing studies to characterize and measure environmentally significant volatile organic pollutants in various sample matrices, we were interested in determining whether these chemicals were present in a patient population whose medical histories suggested a high sensitivity to synthetic chemicals. A second objective was to establish baseline concentration and frequency of occurrence data for six aromatic hydrocarbons and twelve halogenated organics in a selected population. Therefore, we undertook to ascertain the presence of eighteen commonly used organic solvents and vapors in whole blood of environmentally sensitive patients by means of a recently developed clinical screening test known as the VOST™ (volatile organics screening test). What follows is a report of our findings.

MATERIALS AND METHODS

A test population of 250 patients was selected by participating physicians who specialize in the treatment of individuals suffering from a wide variety of symptoms which may be related to an elevated susceptibility to environmental agents. The test group was composed of 121 males and 129 females of various ages. In many cases, these patients had not been exposed to any elevated levels of volatile organics, although some degree of exposure is unavoidable due to the ubiquity of these pollutants in the environment. In other cases, the patients were employed in occupations susceptible to a substantial risk of exposure to elevated levels of organic solvents.

Whole blood specimens were drawn by venipuncture directly into vacutainer tubes (American Scientific Products, Inc.) and were analyzed within 5 days by a purge and trap method similar to one described by Dowty et al. 1979. Briefly, the procedure is as follows:

A 6 ml sample of whole blood was transferred by a glass pipet to a 25 ml glass syringe containing 2 mls of Antifoam Emulsion B (Sigma Chemical Co.) in organic-free water. To the resulting mixture was added a known quantity of xylene-d_{10} as an internal standard. The sample mixture was then placed in the purging vessel of a Model LSC-1 liquid sample concentrator (Tekmar Co.) and purged for 15 minutes with helium at a flow rate of 20 mls/min while maintaining its temperature at 40-50°C by a warm water bath. The volatile organics were swept into a Tenax-GC/silica gel trap (1/8 in. x 12 in. column packed with 2/3 Tenax-GC and 1/3 silica gel). The trapped organics were thermally desorbed at 250°C directly into the gas chromatograph of a Hewlett-Packard (HP) 5985A gas chromatograph/mass spectrometer. The GC oven was maintained at -20°C for the duration of the 6 minute desorption period. Following desorption the column was programmed at 4°C/min to 130°C. The gas chromatographic separations were achieved on a 50 m x 0.3 mm fused silica SE-54 column (Quadrex Corp.). The column effluent was subsequently introduced into the ion source of the mass spectrometer. Sample ionization was by electron-impact at 70 eV. The mass range was scanned repetitively from 35 to 300 amu under computer control using standard HP routines. Mass spectral data analyses were performed by searching for one or more characteristic ions at the expected retention times as determined from standard runs. Complete mass spectra were obtained and examined as required for

verification of identify, particularly in cases of unusually high concentrations. Quantifications were accomplished by integration of extracted ion-current profiles and the application of relative response factors.

RESULTS AND DISCUSSION

The reproducibility of the procedure was tested by the analysis of replicate samples fortified with 2 ng/ml (2 ppb) of each component in the screening test. Coefficients of variation for most of the compounds were less than 5%, a generally considered acceptable level. The linearity of the procedure over the concentration range of 0.5 to 50 ng/ml (ppb) was found to be acceptable, with high correlation coefficients for all compounds tested.

Whole blood specimens were screened for the presence of 6 aromatic compounds (benzene, toluene, ethylbenzene, styrene, xylene, and trimethylbenzene) and 12 halogenated hydrocarbons (dichloromethane, chloroform, carbon tetrachloride, 1,1,1-trichloroethane, trichloroethylene, 1,1,2,2-tetrachloroethane, tetrachloroethylene, bromoform, bromodichloromethane, dibromochloromethane, bromoform, and dichlorobenzene). Thirteen of these volatile organics were routinely observed in the blood samples tested. These include six aromatic organics and seven halogenated organics. Descriptive statistics including means, ranges, and frequency of elevated occurrence for each of these components are presented in Table 1. The mean concentrations for all 250 specimens ranged from 0.4 ng/ml (ppb) for styrene and trichloroethylene to 5.2 ng/ml (ppb) for xylene. The individual concentrations for all components measured ranged from a low of not detected for ten of the components to a high of 160 ng/mL (ppb) for xylene. Of the 250 specimens tested, 65 had one or more components present at a concentration greater than or equal to 2 standard deviations above the mean. Thus, the majority of the specimens were judged to be not statistically significant from one another. Accordingly, their means may be used as an estimate of baseline levels for the test population. In several instances, the blood levels of volatile organics were significantly higher than the mean suggesting a specific occupational or environmental exposure. Two selected cases illustrate this.

The first case was traced to an occupational exposure and involved 16 wire workers employed at a wire-manufacturing company. The company was under investigation by authorities because of widespread illness among the employees, and had previously been cited for excessive

Table 1. Average, range and frequency of eleveated occurrence of volatile organics in 250 whole blood specimens

Compound	Mean expressed in ng/ml (ppb)	Range expressed in ng/ml (ppb)	Number of times significantly elevated[a]
Benzene	0.8	N.D.[b] 5.9	10
Toluene	1.5	0.2 - 38.	3
Ethylbenzene	1.0	N.D. - 59.	3
Xylene	5.2	0.5 -160.	7
Trimethylbenzene	0.8	N.D. - 46.	3
Styrene	0.4	N.D. - 1.9	6
Dichlorobenzene	0.6	N.D. - 31.	6
Dichloromethane	0.7	N.D. - 25.	3
Chloroform	1.5	N.D. - 7.0	9
Bromoform	0.6	N.D. - 3.4	11
1,1,1-Trichloroethane	1.0	N.D. - 26.	5
Trichloroethylene	0.4	N.D. - 1.5	13
Tetrachloroethylene	2.4	0.7 - 23.	8

[a]Number of cases out of 250 that compound was present at a concentration greater than 2 standard deviations above the mean.
[b]N.D. means not detected.

combined workspace concentrations of xylene, phenol and cresol. A volatile organics profile comparing the mean concentrations for these workers to the mean concentrations for the remainder of the test population is shown in Figure 1. All of the aromatic hydrocarbon means in the wire workers profile are greater than the means of the remainder of the population, suggesting a direct occupational relationship. In order to test the hypothesis that the data for the two groups differ significantly from each other, an analysis of variance was performed. F ratios were computed, where F = between-groups mean square/within-group mean square, followed by determination of the significance level to which these F values correspond, based on the degrees of freedom. The mean values for the 16 workers were significantly higher than the mean value for remainder of the population for benzene, ethylbenzene, xylene, trimethylbenzene, and dichlorobenzene. Xylene, for example, was significanty elevated (at $p \leq 0.05$) in the blood of 6 of the 16 workers tested. The highest xylene value detected was 160 ng/ml (ppb), more than 30 times the average value for xylene in the test population. In one of the workers, the value of di-

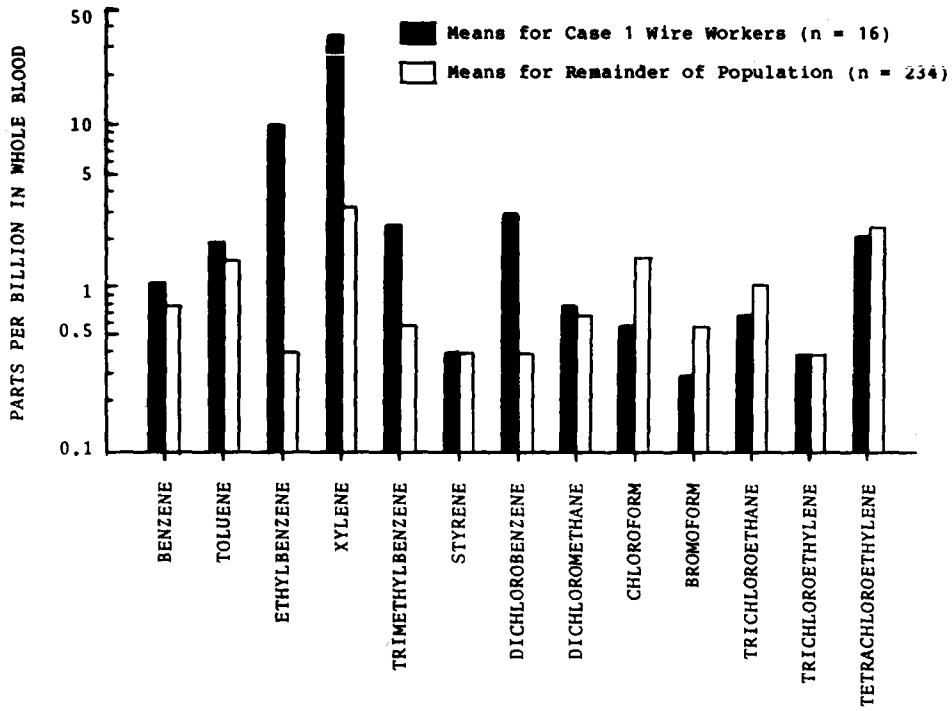

Figure 1. Comparison of the mean blood volatile organics in exposed wire workers vs. test population

chlorobenzene (31 ng/ml) was more than 12 standard deviations greater than the mean. Similar observations of elevated values were made for all 16 workers in this case.

The second case involved an individual whose exposure was determined to be related to drinking water contamination. In 1981, municipal wells in this patient's area of residence were found to be contaminated by

various volatile organics including trichloroethane and trichloroethylene at the parts-per-million level. Because this patient utilized municipal water as his drinking water supply, it was of interest to determine his volatile organics profile in blood relative to time. In the initial sampling, this patient had a level of 1,1,1-trichloroethane in the blood of 5.2 ng/ml (at $p \leq 0.07$). The total volatiles were 20 ppb and chlorinated hydrocarbons made up 70% of that total. The patient then switched to another drinking water supply following the initial sampling. In the second specimen, collected two weeks after the initial sampling, chlorinated hydrocarbons made up only 53% of the total volatiles, with the total volatiles showing a drop of almost 50%. Trichloroethane levels had decreased from 5.2 ppb to less than 1 ppb and all other volatile organics were at concentrations either equal to or less than those found in the previous sampling. The third specimen, taken almost 3 months after the initial sampling, showed even a greater drop in the volatile organics levels. Total volatiles were only 5.3 ppb and chlorinated hydrocarbons made up only 45% of this total. Other specimens analyzed concurrently with specimens in this case did not show similar differences. A comparison of the results for the three samples are shown in Figure 2. In all instances after the initial specimen, the measured components decreased in value as expected, once the ingestion of contaminated drinking water was stopped.

All thirteen of the volatile organic components which were identified and measured in the blood specimens of the test population are environmentally significant chemicals with quite variable physical, chemical, and toxicological properties which allow for a variety of commercial and industrial applications. These chemicals are used extensively as solvents, chemical intermediates, dewaxing agents, aerosol propellants, blowing agents, pharmaceuticals, etc. (Clayton and Clayton 1981 and Verschueren 1977). Among the possible adverse human health effects reported due to exposure to these chemicals are irritation of the skin, eyes, and respiratory tract, central nervous system depression, narcosis, memory impairment, fatigue, personality changes, headaches, dizziness, various renal and hepatotoxic effects, and even hematologic damage (Clayton and Clayton 1981, Christensen et al. 1975; Verschueren 1977, Baselt 1982). However, many aspects of the metabolism and toxic effects of these chemicals have not been fully studied or documented. Included are aspects related to synergism, sensitization, and the wide variability of individual behavioral, biochemical, and physiological responses to these toxicants. Therefore, it is difficult to determine the

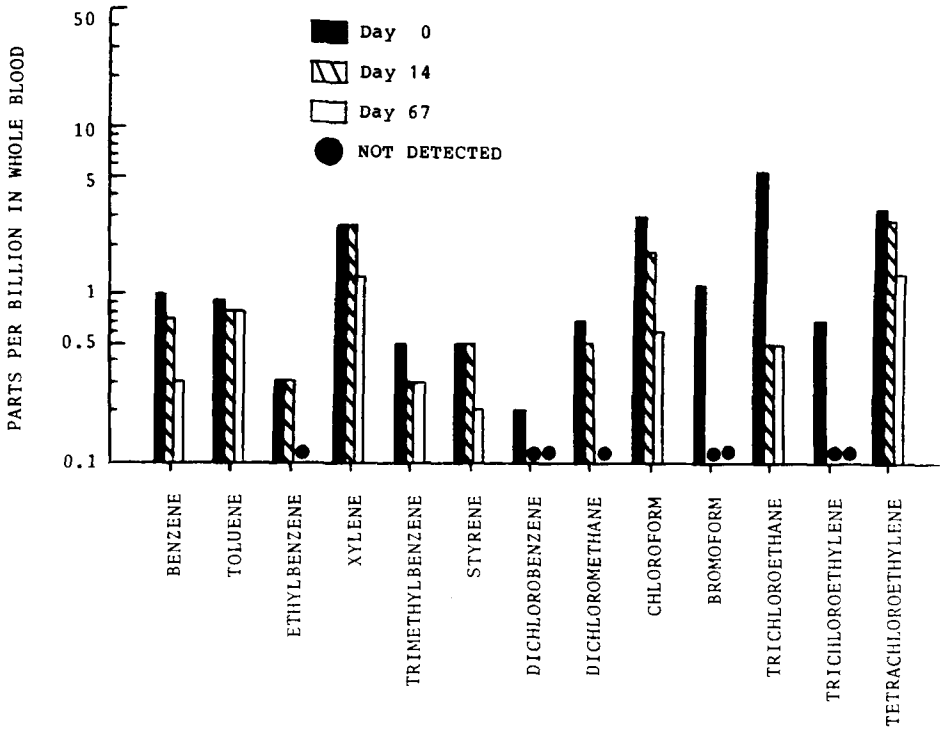

Figure 2. Blood volatile organics profiles for Case 2 showing initial specimen (Day 0) and specimens taken on Day 14 and Day 67.

degree, if any, to which elevated levels of volatile organic compounds contribute to health problems in cases of occupational or environmental exposures.

The data which have been developed in this study show the presence of thirteen environmentally significant volatile organics in the blood specimens of the test population and provide indices which may be used as blood baseline values for these toxicants. The data

further demonstrate that a definitive description of volatile organics body burden is possible and that cases of elevated blood volatile organics may be isolated and traced to possible sources in the environment. The extent to which these environmental pollutants, at the levels determined, affect the health of the individual cannot be assessed until more detailed studies are conducted.

Acknowledgements. The authors gratefully acknowledge the discussions and encouragement of J.L. Laseter, S.E. Bryan, J.E. Utley, and thank K.D. Trembley for expert assistance in the preparation of this manuscript.

REFERENCES

Baselt RC (1982) Disposition of toxic drugs and chemicals in man. Biomedical Publications, Davis, CA

Clayton GD, Clayton FE (eds.) (1981) Patty's industrial hygiene and toxicology, Volume 2B. John Wiley and Sons Inc., New York

Christensen HR, Luginbyhl TT, Carroll BS (1975) Registry of toxic effects of chemical substances. U.S. Department of Health, Education and Welfare, Report # CDC 99-74-92

Dowty, B, Carlisle D, Laseter JL, Storer J (1975a) Halogenated hydrocarbons in New Orleans drinking water and blood plasma. Science 187:75-77.

Dowty, B, Laseter JL (1975) A gas chromatographic procedure to monitor low molecular weight volatile organics introduced during municipal water processing. Anal Lett 8:25-32

Dowty BJ, Antoine SR, Laseter JL (1979) Quantitative and qualitative analysis of purgeable organics by high-resolution gas chromatography and flame ionization detection. In Van Hall CE (ed.) Measurement of organic pollutants in water and wastewater, ASTM STD 686. ASTM, Philadelphia, 24-35

Dowty BJ, Carlisle D, Laseter JL, Gonzalez FM (1975b) Gas chromatographic mass spectrometric computer analysis of volatile components in blood plasma from hemodialysis patients. Biomed Mass Spectrom 2:142-147

Dowty BJ, Green LE, Laseter JL (1976a) Automated gas chromatographic procedure to analyze volatile organics in water and biological fluids. Anal Chem 48:946-949

Dowty BJ, Laseter JL, Storer J (1976b) The transplacental migration and accumulation in blood of volatile organic constituents. Pediat Res 10:696-701

Laseter JL, Dowty BJ (1977) Association of biorefractories in drinking water and body burden in people. Ann NY Acad Sci 298:547-556

Verschueren K (1977) (ed) Handbook of environmental data on organic chemicals. Van Nostrand Reinhold Co, New York

Received March 4, 1985; accepted March 25, 1985.