Individuals are exposed to volatile compounds present in tap water by ingestion, inhalation, and dermal absorption. Traditional risk assessments for water often only consider ingestion exposure to toxic chemicals, even though showering has been shown to increase the body burden of certain chemicals due to inhalation exposure and dermal absorption. We collected and analyzed time-series samples of expired alveolar breath to evaluate changes in concentrations of volatile organic compounds being expired, which reflects the rate of change in the bloodstream due to expiration, metabolism, and absorption into tissues. Analysis of chloroform and trichloroethene in expired breath, compounds regulated in water, was also used to determine uptake from tap water by each route (ingestion, inhalation, and dermal absorption). Each route of exposure contributed to the total exposure of these compounds from daily water use. Further, the ingestion dose was completely metabolized before entering the bloodstream, whereas the dose from the other routes was dispersed throughout the body. Thus, differences in potential biologically effective doses depend on route, target organ, and whether the contaminant or metabolite is the biologically active agent.

**Key words:** chloroform, dermal exposures, drinking water, ingestion exposures, inhalation exposures, trichloroethene, volatile organic compounds. *Environ Health Perspect* 104:48-51 (1996).

Metabolism of environmental contaminants occurs in multiple organs, and the site of metabolism is an important determinant of a compound’s toxicity. The route of exposure can alter the overall rate and site of metabolism and affect a compound’s site-specific toxicity.

The concentration of a volatile compound in exhaled breath is related to its concentration in the bloodstream and can be used to determine changes in body burden with time (8-10). Exhaled breath concentrations have also been used to infer the relative internal dose received, the exposure route, and to examine differences in overall metabolic rates (11-13). Physiologically based pharmacokinetic (PBPK) models are used to model the distribution of environmental contaminants and their metabolites in the body (14,15). An application of a PBPK model by Blancto and Chiu (15) examined the biologically effective dose resulting from exposure to contaminants in water and predicted that for the same amount of internalized chloroform, ingestion exposure results in a higher dose of chloroform to the liver, but inhalation and dermal absorption exposure results in more chloroform being circulated throughout the body and to other organs, such as the bladder. Epidemiological studies examining the health effects of chlorinated water have found that populations exposed to chlorination by-products have elevated bladder cancer rates (16,17) and have suggested an association between exposure to chlorination by-products in water and adverse reproductive outcomes (18,19).

The present research was conducted to determine the dose of water contaminants resulting from the three common routes associated with water use: ingestion (drinking), inhalation (during showering), and dermal contact (showering, bathing). The results were based on measurements of human breath concentrations of chloroform and trichloroethene following ingestion, inhalation, and dermal exposures to residential tap water. Chloroform is contained in municipal water supplies that are disinfected by chlorination, the most common disinfection process in the United States (20). Trichloroethene is a common contaminant in groundwater, particularly near National Priority List or Superfund sites (21). To obtain the incremental dose, each experiment was limited to examining a single exposure route.

**Methods**

Exposure to a single route at a time was accomplished by imposing a control on the routes of exposure not being studied while performing normal activities (drinking, showering, and bathing) (4). During an inhalation exposure, the subject wore waterproof clothing while showering to minimize dermal contact. For dermal exposure, the subject breathed purified air while showering or bathing. The compounds were then measured in a time series of exhaled breath samples to monitor their expiration rate.

We performed 25 experiments using 11 subjects (6 males and 5 females between the ages of 20 and 50 years old). Eight 10-min dermal-only "showerers" and four 60-min dermal-only baths were taken to evaluate the effect of the dermal exposure route on the elimination rates of volatile organic compounds (VOCs). Nine 10-min inhalation experiments were conducted using 4 subjects (2 males and 2 females between the ages of 20 and 50 years old). Eight 10-min dermal-only "showerers" and four 60-min dermal-only baths were taken to evaluate the effect of the dermal exposure route on the elimination rates of volatile organic compounds (VOCs). Nine 10.min inhalation experiments were conducted using 4 subjects (2 males and 2 females between the ages of 20 and 50 years old).

Address correspondence to C.P. Weisel, Environmental and Occupational Health Sciences Institute, UMDNJ-Robert Wood Johnson Medical School, 675 Hoes Lane, Piscataway, NJ 08854 USA.

This work was supported by the Risk Science Institute-ILSI, NIEHS Superfund Basic Research Program (project ES-05995), and an NIEHS center grant (ES05022-06).

Received 18 July 1995; accepted 11 October.
tion-only showers were taken to evaluate the effect of the inhalation exposure route on elimination rates of VOCs. Four experiments were performed for ingestion of 0.5 l water. Informed consent was obtained from each subject.

Water samples were collected into clean glass vials with teflon-lined enclosures. During collection, care was taken to ensure that no bubbles formed in the water. The water was analyzed for chloroform and trichloroethene by purge and trap followed by GC/MS or GC/electron capture detection (ECD). The air was sampled during the entire inhalation exposure by drawing an air sample through a 0.25-inch ID stainless-steel trap packed with a multilayered, adsorbent trap containing Carboxen 563 (Supelco Co., Bellefonte, Pennsylvania), Tenax TA (Alltech Corp., Deerfield, Illinois), and Carbosieve III (Supelco). Breath samples were collected using a sampler designed to collect primarily alveolar air (11). The subject breathed through a new mouthpiece into a one-way valve that directed the inspired air from a charcoal purifier into the subject and the expired air into a temporary storage tube (0.64 cm x 8 m) from which the breath was continually withdrawn onto an adsorbent trap using a personal sampling pump set at a flow rate of 1 l/min. A series of breath samples were collected after exposure at times ranging from between 1 min and several hours to determine the relative body burden of chloroform or trichloroethene resulting from each exposure. The air and breath samples were analyzed by thermal desorption coupled with GC/MS or GC/ECD. During the inhalation and dermal exposures, the shower and bath water was maintained at a temperature of 40 ± 2°C, a typical water temperature for bathing.

**Results and Discussion**

Only the breath samples collected seconds to minutes after ingestion residential well water containing trichloroethene had elevated concentrations of trichloroethene. Following ingestion of chlorinated municipal water, none of the breath samples had measurable levels of chloroform. The initial elevation of breath concentrations for trichloroethene is most likely due to off-gassing of VOCs from the residual water present within the oral cavity, rather than reflecting blood-air exchange in the alveolar sacs because no continued elevation was detected. One explanation for this observation is that the internal dose received from ingestion is completely metabolized during a first pass through the liver, thus there was no measurable elevation in VOC concentration in the exhaled breath, which would reflect elevated blood concentrations.

The chloroform and trichloroethene concentrations in the exhaled breath were elevated in each subject after both inhalation and dermal exposures during showering, demonstrating that chemicals in the water entered the body by both routes (Figures 1 and 2). Breath concentrations were also elevated after dermal exposure via bathing (Fig. 1C). In contrast to ingestion, after inhalation and dermal exposure, the exhaled breath had elevated levels for extended time periods, implying that the compounds were distributed throughout the bloodstream before being metabolized. These observations support the predictions of a PBPK model for chloroform exposures from tap water (15).

One previous study measured elevated levels of chloroform in blood and breath following a bolus ingestion of 5 x 10³ µg (0.5 g) of chloroform (22). The present study used a total ingestion of only 10 µg of chloroform (0.5 l water containing 20 µg/l) and 10 or 20 µg of trichloroethene (0.5 l water containing 20 or 40 µg/l), common environmental levels. The 0.5-g ingestion probably exceeded the metabolic capacity of the liver. Thus, a portion of chloroform was metabolized during the first pass through the liver and entered the circulatory system, whereas the ingestion of environmentally relevant concentrations are unlikely to have saturated metabolic enzymes. These data imply that for common environmental levels, if the target organ of a waterborne contaminant is the liver or if a long-lived metabolite is the toxic agent, then an ingestion exposure delivers the largest biologically effective dose via the three routes studied. However, if a different organ is the target, and either the parent compound or a short lived metabolite is the biologically active agent, then inhalation and dermal exposures would deliver a larger biologically effective dose than ingestion. For example, for chloroform, the reactive metabolite phosgene is suspected to be the biological active agent (23); thus, inhalation and dermal absorption exposures to chlorinated water will result in a larger chloroform dose and may present a greater risk than ingestion to organs other than the liver, such as the bladder where elevated cancer rates have been suggested (16,17), and for adverse reproductive outcomes (18-20).

The amount of chloroform expired per microgram of the compound in 1 l of water was calculated from the expired breath profiles, assuming a respiration rate of 0.01 m³/min. These values ranged from 0.02 to 0.05 µg for the inhalation-only exposure (Fig. 1A), from 0.02 to 0.13 µg for the dermal-only shower exposure (Fig. 1B) and...
from 0.33 to 0.56 μg after the dermal bathing study (Fig. 1C). The larger amount expired after bathing is due to the longer exposure time (60 min versus 10 min for the shower) and a larger portion of the body surface being in constant contact in the water. The amount of trichloroethene expired per microgram of the compound in 1 l of water after the inhalation exposure (Fig. 2A) was 0.074 ± 0.080 μg and after dermal exposure (Fig. 2B) was 0.030 ± 0.011 μg. However, the amount of trichloroethene expired after one of the inhalation exposure experiments is an order of magnitude higher than the other values. If that value is removed, the mean trichloroethene expired after inhalation exposure was 0.035 ± 0.018 μg, which was equivalent to the dermal value. The expiration data directly demonstrate that dermal exposure contributes as much to the body burden of chloroform or trichloroethene as inhalation exposure while showering with water containing these contaminants. Extended bathing yields an even greater dermal dose.

The internal dose derived from inhalation can be calculated from the air concentration, breathing rate, duration of the shower, and adsorption efficiency across the lung barrier (9). The calculated internal dose from inhalation exposure ranged between 60 and 250 μg for trichloroethene and between 30 and 80 μg for chloroform. The amount of chloroform and trichloroethene expired after inhalation and dermal shower exposures were similar, suggesting nearly equivalent internal doses for these two exposure routes during showering. An ingestion of 2 l of water containing the concentrations observed in this study and, assuming a 100% transfer across the gastrointestinal tract, yields maximum internal dose estimates for trichloroethene of 30–300 μg and for chloroform of 10–100 μg. Thus, for typical activities of drinking and showering, each exposure route contributes similar internal doses, and the total internal dose from a 10-min shower or a 30-min bath is greater than that from ingesting 2 l of water.

In conclusion, approximately equivalent amounts of volatile contaminants from water can enter the body by three different exposure routes, inhalation, dermal absorption, and ingestion, for typical daily activities of drinking and bathing. However, the exposure route affects the rates of metabolism and therefore the compound’s potential toxicity. The ingested VOCs were metabolized during the first pass through the liver, thus the parent compound was not measurable in the exhaled breath and would not be present in the bloodstream. However, chloroform and trichloroethene concentrations were measurable in the breath after inhalation and dermal exposure, indicating dispersion throughout the body. These results confirm the necessity of knowing the biologically active agent (either the parent compound or a metabolite of VOCs found in water) and the site of activity of a contaminant to accurately quantify the dose received from all significant exposure routes before forming public health policies related to contaminated water supplies.

REFERENCES

1. Vanderslice RR. Benefits of deriving drinking water standards based on comprehensive assessments of exposure. In: Water contamination and health (Wong R, ed). New York: Marcel Dekker, 1994:125–134.

2. U.S. EPA. Workshop on assessment and management of drinking water contamination. EPA/600/M-86/026. Washington, DC: Environmental Protection Agency, 1987.

3. Jo WK, Weisel CP, Liow PJ. Routes of chloroform exposure and body burden from showering with chlorinated tap water. Risk Anal 10:575–580 (1990).

4. Jo WK, Weisel CP, Liow PJ. Chloroform exposure and the health risk and body burden from showering with chlorinated tap water. Risk Anal 10:581–585 (1990).

5. Andelman J. Inhalation exposure in the home to volatile organic contaminants of drinking water. Sci Total Environ 47:463–466 (1985).

6. McKone TE. Human exposure to volatile organic compounds in household tap water: the indoor inhalation pathway. Environ Sci Technol 21:1194–1201 (1987).

7. Maxwell NI, Burmaster DE, Ozone off. Trihalomethanes and maximum contaminant levels: the significance of inhalation and dermal exposures to chloroform in household water. Regul Toxicol Pharmacol 14:297–312 (1991).

8. Brugnone F, Perbellini L, Facchin GB, Pani F, Danzi B, Maranelli G, Romeo L, Govi M, Zedda A. Benzenoid and trichloroethene and the blood and breath of normal and occupationally exposed workers. Am J Ind Med 16:385–399 (1989).

9. Weisel CP, Jo WK, Liow PJ. Utilization of breath analysis for exposure and dose estimates of chloroform. J Expo Anal Environ Epidemiol 1:55–69 (1992).

10. Petreas MX, Rappaport SM, Maretta BL, Rempl DL. Mixed-exhaled air measurements to assess exposure to tetrachloroethylene in dry cleaners. J Expo Anal Epidemiol (Suppl) 1:25–39 (1992).

11. Raymer JH, Pellizzari ED, Thomas KW, Cooper SD. Elimination of volatile organic compounds in breath after exposure to occupational and environmental microenvironments. J Expo Anal Epidemiol 1:439–451 (1991).

12. Gordon SM, Kenny DV, Kelly TJ. Continuous real-time breath analysis for the measurement of half-lives of expired volatile organic compounds. J Expo Anal Epidemiol 1:41–54 (1992).

13. Wallace L, Pellizzari ED, Gordon S. A linear model relating breath concentrations to environmental exposures: Application to a chamber study of four volunteers exposed to volatile organic chemicals. J Expo Anal Epidemiol 3:75–102 (1993).

14. McKone TE. Linking a PBPK model for chloroform with measured breath concentrations in showers: Implications for dermal exposure models. J Expo Anal Epidemiol 3:339–365 (1993).

15. Blancto JN, Chiu N. Predictive modeling for uptake and tissue distribution from human exposures. In: Safety of water disinfection: balancing chemical and microbial risks (GF Craum, ed). Washington, DC: LSI Press, 1993:303–316.

16. Cantor KP, Hoover R, Harget P, Mason TJ, Silverman DT, Altman R, Austin DF, Child MA, Key CR, Marquet LD, et al. Bladder cancer, drinking water source, and tap water consumption: a case-control study. J Natl Cancer Inst 79:1269–1279 (1987).

17. McGeehin MA, Reif JS, Becher JC, Mangione EJ. Case-control study of bladder cancer and water disinfection methods in Colorado. Am J Epidemiol 138:492–501 (1993).

18. Kramer MD, Lynch CF, Isacson P, Hanson JW. The association of waterborne chloroform

Volume 104, Number 1, January 1996 • Environmental Health Perspectives
with intrauterine growth retardation. Epidemiology 3:407–413 (1992).
19. Bove F, Fulcomer MC, Savrin JE. Public drinking water contamination and birth outcomes. Am J Epidemiol 141:850–862 (1995).
20. Krasner SW, McGuire MJ, Jacangelo JG, Patania NL, Reagan KM, Aieta EM. The occurrence of disinfection by-products in US drinking water. J Am Water Works Assoc 81:41–53 (1989).
21. ATSDR. Toxicological profile for trichloroethylene. TP-92/19. Atlanta, GA: Agency for Toxic Substances and Disease Registry, 1993.
22. Fry BJ, Taylor T, Hathway DE. Pulmonary elimination of chloroform and its metabolite in man. Arch Int Pharmacodyn 196:98–111 (1972).
23. Davidson IW, Summer DD, Parker JC. Chloroform: a critical review of its metabolism, teratogenic, mutagenic and carcinogenic potential. Drug Chem Toxicol. 5:1–87 (1982).

41st Annual Institute in Water Pollution Control

Manhattan College
Riverdale, NY
June 3–7, 1996

Manhattan College’s forty-first annual Institute in Water Pollution Control will take place on June 3–7, 1996 in the Manhattan College Leo Engineering Building, Riverdale, New York. Two courses, which run concurrently, will be offered: Modern Eutrophication Modeling, and Treatment of Municipal, Hazardous and Toxic Wastewaters. These week-long courses have much to offer young engineers and seasoned professionals who have not been able to stay abreast of the rapidly changing field. Set in a classroom atmosphere, the courses allow for dialog between lecturer and participants. The fee per course is $1,150 and includes a set of notes for each attendee.

For a brochure of additional information, contact:

Ms. Lucia Chiocchio, Program Coordinator
Manhattan College
Environmental Engineering Department
Riverdale, NY 10471
Phone (718) 920-0277
FAX (718) 543-7914