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ENVIRONMENTAL AND BIOMARKER MEASUREMENTS IN NINE HOMES IN THE LOWER RIO GRANDE VALLEY: MULTIMEDIA RESULTS FOR PESTICIDES, METALS, PAHs, AND VOCs

T.J. Buckley*
U.S. EPA, National Exposure Research Laboratory (MD-56), Research Triangle Park, NC 27711, USA

J. Liddle, D.L. Ashley, D.C. Paschal, V.W. Burse, and L.L. Needham
Centers for Disease Control and Prevention, Division of Environmental Health Laboratory Sciences (MS F-20), Atlanta, GA 30333, USA

G. Akland
U.S. EPA, National Exposure Research Laboratory (MD-56), Research Triangle Park, NC 27711, USA

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Residential environmental and biomarker measurements were made of multiple pollutants during two seasons (spring and summer, 1993) in order to assess human exposure for a purposeful sample of 18 nonsmoking adults residing within nine homes (a primary and secondary subject in each home) in the Lower Rio Grande Valley (LRGV) near Brownsville, TX. Pesticides, metals, PAHs, VOCs, and PCBs were measured in drinking water, food, air, soil, and house dust over a one- to two-day period in each season. Biomarker measurements were made in blood, breath, and urine. A total of 375 measurements across five pollutant classes (227 pesticides, 44 trace elements, 78 VOCs, 18 PAHs, and 8 PCBs) was possible for each home in one or more media. A large percentage of the measurements was below the method limit of detection ranging from 0-37% for pesticides, 22-61% for metals, 6% and 90% for VOCs in water and air, respectively, and 0-74% for PAHs. The total number of analytes measurable in blood, urine, or breath was considerably less, i.e., 58 (21 pesticides, 1 PCB, 4 metals, 31 VOCs, and 1 PAH) with the percentage above the method limit of detection for pesticides and metals ranging from 40 to 100%, while for VOCs, PAHs, and PCBs, this percentage ranged from 2 to 33%. A significant seasonal difference ($p \leq 0.10$) was found in the biomarker levels of two of seven nonpersistent pesticides (3,5,6-trichloro-2-pyridinol and 2,5-dichlorophenol) and 3 of 3 metals (arsenic, cadmium, and mercury) and the pyrene metabolite, 1-hydroxypyrene, measured in urine. In all cases, levels were higher in the summer relative to the spring. For the persistent pesticides and PCBs in blood serum, a seasonal effect could be evaluated for 5 of 10 analytes; a significant difference ($p \leq 0.10$) was observed only for hexachlorobenzene, which like the urine biomarkers, was higher in the summer. In contrast to the urine metals, blood-Pb concentrations did not change significantly ($p \leq 0.05$) from spring to summer. Biological results from the current study are compared to the reference range furnished by the Third National Health and Nutrition Examination Survey (NHANES III). Comparisons are only suggestive due to limitations in comparability between the two studies. Based on the percentage of measurements above the detection limit, a significant elevation ($p \leq 0.10$) in 2 of 12 nonpersistent pesticides (4-nitrophenol and 2,4-D) was observed for the LRGV study subjects. The VOC carbon tetrachloride was found in the blood (monitored only in spring) with greater prevalence ($p \leq 0.10$) than would be expected from NHANES III results. Blood serum levels of two persistent pesticides (4,4'-DDE, and trans-nonachlor) and PCB exceeded median and/or 95th

*Current address: Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Md 21205, USA.

percentile reference levels as did arsenic in urine. Where seasonal differences were identified or for compounds exceeding reference levels, environmental monitoring results were investigated to identify potential contributing pathways and sources of exposure. However, because environmental sampling did not always coincide with the biological sampling and because of the high frequency of analytes measured below the limit of detection, sources and pathways of exposure in many cases could not be explained. Chlorpyrifos was an exception where urine metabolite (3,5,6-TCP) levels were found to be significantly correlated with air (R^2=0.55; $p \leq 0.01$) and dust (R^2=0.46; $p \leq 0.01$) concentrations. Based on the results of biomarker and residential environmental measurements over two seasons, this scoping study shows a seasonal effect for some analytes and suggests where exposures may be high for others. This information may be useful in considering future studies in the region. Published by Elsevier Science Ltd

INTRODUCTION

The Lower Rio Grande Valley Environmental Exposure Scoping Study (LRGVES) was a community-based exposure study designed to respond to community environmental health concerns, test exposure assessment methods, characterize ranges and pathways of exposure, and support the design of a large-scale human exposure study planned for the region. This paper presents an integrated overview of biomarker and residential-based environmental measurement results.

The overarching context for the study was exposure assessment as it exists within a risk framework (NRC 1983; Lippmann and Thurston 1988). All exposures potentially contributing to body burden, and consequently to a health effect, were of interest regardless of exposure route or pathway. This integrated approach to human exposure assessment has been described and justified by Ott (1990) and Lioy (1990). Examples of studies using this approach for single classes of pollutants include the Total Exposure Assessment Methodology for VOCs (TEAM-VOC), the Non-occupational Pesticide Exposure Study (NOPES), and the Total Human Environmental Exposure Study (THEES) for PAHs described by Wallace et al. (1986), Whitmore et al. (1994), and Buckley et al. (1995), respectively. The LRGVES was designed with this conceptual notion of exposure in mind. Accordingly, monitoring was conducted to account for all relevant routes (inhalation, ingestion, and dermal absorption) and pathways (air, water, food, dust, and soil) of exposure. This strategy usually relies on the coupling of external measures of exposure with measurements of the contaminant (or their metabolites) within body compartments (e.g., blood, urine, breath) (U.S. EPA 1988; NRC 1991a; Pirkle et al. 1995). The importance of this approach for reducing uncertainty in risk assessment is well established (Sexton et al. 1995; NRC 1991b, 1991c). The combination of biomarkers and multi-media environmental measurements is especially valuable in identifying exposure pathways and sources that contribute to body burden and effects from which effective exposure reduction strategies can be developed.

The Lower Rio Grande Valley community was concerned that they were being affected by emissions from the maquilladora plants across the river although no specific etiological agents were identified. The U.S. EPA responded to this concern with a monitoring strategy that was broad-based – encompassing multiple pollutants in multiple environmental and biological media. The study's goal was to generally characterize pollutant levels to provide possible indications of contamination that might lead to high exposures and warrant further investigation. These results would be considered in the design of the larger follow-up study. Accordingly, monitoring methods that would give broad results within and across pollutant classes were employed and, where necessary, developed and validated (Mukerjee et al. 1997a; Berry et al. 1997b). In addition, this broad multimedia monitoring approach provided the opportunity to investigate exposure associations across different pathways and pollutant classes so that the cumulative environmental exposure insult could be potentially evaluated. This strategy of considering multiple chemical insults from multiple pathways of exposure and engaging community stakeholders as partners in the study design and implementation has been recognized by the Presidential/Congressional Commission on Risk Assessment and Risk Management (1997) as effective in supporting risk assessment and management.

Consequently, the scope of this monitoring effort was of unprecedented breadth. Five pollutant classes (pesticides, PCBs, metals, VOCs, and PAHs) were monitored in five environmental media (food, drinking water, air, house dust, and soil) and three biological matrices (blood, breath, and urine). A total of 227

pesticides, 44 trace elements, 78 VOCs, 18 PAHs, and 8 PCBs were measured across the various media. However, because analytes were not always consistently measured across all the relevant media and because a large number of measurements were below the limit of detection, complete multimedia assessments were rarely possible. Chlorpyrifos was an exception. With a vapor pressure of 2×10^{-5} mm Hg at 25°C (Racke 1993), chlorpyrifos was found at levels above detection in indoor air and house dust as has been previously observed (Camann et al. 1990; Roinestad et al. 1993; Whitmore et al. 1994; Lewis et al. 1994; Fenske et al. 1990). As Fenske and Elkner (1990) observed in commercial home applicators, with an R^2 of 0.86, the urinary metabolite 3,5,6-trichloro-2-pyridinol (3,5,6-TCP) appears to be an effective biomarker for exposure.

The pyrene metabolite, 1-hydroxypyrene (1-OHPY), was the single PAH biomarker measured in the current study. The validity of 1-OHPY to distinguish groups differentially exposed is well established (Levin et al. 1995; Viau et al. 1995; Göen et al. 1995). Seasonal variability in 1-OHPY elimination has been reported by Zhao et al. (1992) for residences in Beijing where winter was observed to be significantly ($p \leq 0.01$) higher than summer, although the applicability of these findings to the current study are tenuous due to climate and cultural differences between the study locations. Diet has been shown to be a dominant pathway of exposure for PAH (Buckley and Lioy 1992; Buckley et al. 1995).

Seasonal trends in biomarker measurements can be an important consideration in the design and interpretation of exposure or epidemiologic studies. This trend is well characterized for blood-Pbs in children based on a study in Boston where blood-Pb concentrations were observed to be highest in late June and lowest in March (U.S. EPA 1995). Similarly, in the NOPES, Whitmore et al. (1994) observed that environmental pesticide concentrations tended to be highest in the summer, lowest in the winter, with spring levels lying in between for the two cities studied (Jacksonville, FL, and Springfield/Chicopee, MA). Although no seasonal trend in persistent pesticide serum levels was detected from the Third National Health and Nutrition Examination Survey (NHANES II), Stehr-Green (1989) showed that increasing age, residing on a farm or being male were statistically significant risk factors for elevated levels. This study also revealed factors especially relevant to our Lower Rio Grande sample, i.e., non-white people living below the poverty level who reside in the South or West or who were examined in the spring or winter, were more likely to have quantifiable serum pesticide levels.

Biomarker results were compared to the NHANES II and III reference values as a means to assess the relative level of exposure in the study sample. When NHANES data were not available for comparison (i.e., arsenic, mercury, and cadmium), then alternate reference ranges were considered (Kalman et al. 1990; Clarkson et al. 1988; Wyowski et al. 1978). Similar comparisons with reference biomarker and exposure values may be possible in the future once these data become available through the National Human Exposure Assessment Survey (NHEXAS) pilot studies that are currently underway (Lebowitz et al. 1995; Pellizzari et al. 1995). Through comparisons with such reference data, it may be possible to identify those that are highly exposed warranting further investigation and/or intervention (e.g., PCBs and fishing, Akland et al. 1997). Because of the availability of NHANES national reference data on levels of xenobiotics in blood and urine (Hill et al. 1995; Ashley et al. 1994; Murphy and Harvey 1985), the current study's biomonitoring results formed the cornerstone for evaluating the relative level of exposure for the participants in the nine homes sampled. The goal of this paper is to present the scope and general findings of the LRGVES as they relate to exposure biomarkers.

METHODS

The study's scoping objectives were most effectively achieved by the purposive selection of study participants. Nine homes were selected in and around Brownsville, TX. Five of the homes were in Brownsville and four homes were located West and North of Brownsville along Highway 281, which parallels the Rio Grande River. All homes were within 8 km (5 mi) of the Rio Grande River and the U.S. Mexican border.

Two nonsmoking respondents were selected from each of the 9 homes for a total of 18 subjects. Homes were selected where at least one of the subjects was primarily at home. This subject was designated as "primary". The second subject—designated as "secondary"—typically spent less time at home, e.g., at school or work. The method and rationale for residence and subject selection are more fully described by Akland et al. (1997). All participating subjects gave informed

consent. The consent form and all procedures involving study subjects were approved by the Research Triangle Institute's Institutional Review Board (RTI, Research Triangle Park, NC). Human studies' administrative approval was obtained from both the U.S. EPA and the Centers for Disease Control and Prevention.

The residential monitoring was conducted from 18 March to 9 April (spring phase) and again from 21 July to 3 August (summer phase) 1993. All of the 9 homes and 18 subjects participated in the spring study phase. Of these nine homes, six were available and agreed to participate in a second summer phase, again with the same primary and secondary subjects selected. The study participants are briefly described in Table 1. All of the 18 participants identified themselves of Hispanic ethnicity. Twelve of the participants were females and six were males. The median age was 42 y. Akland et al. (1997) provides additional information on the subjects and their socioeconomic status.

The environmental monitoring was residential-based. Monitoring was linked to the primary and secondary subjects in each home. Since food and beverage samples were collected by "duplicate diet" and this sampling method was considered too burdensome and costly for two samples from each home, this sample was collected only from the primary respondent. Five pollutant classes (pesticides, metals, VOCs, PAHs, and PCBs) were monitored in five environmental media and three biological matrices (Table 2). A total of 227 pesticides, 44 metals, 78 VOCs, 18 PAHs, and 8 PCBs were measurable in one or more of the various environmental media. The specific analytes measured in air, soil, and house dust can be found in Mukerjee et al. (1997b) while the analytes measured in drinking water and diet are reported by Berry et al. (1997a, 1997b), respectively. Subsets of these analytes (or their metabolites) were measurable in blood, urine, and/or breath: 12 nonpersistent pesticides, 10 persistent pesticides (including PCB), 4 metals, 32 VOCs, and 1 PAH. The specific analytes measured in biological matrices are reported in the results section. These samples were collected for both subjects although the urine collection protocol differed between the primary and secondary as described in the urine collection method below.

For many of the pesticides, results are reported according to the measured metabolite. The nonpersistent and persistent pesticides (including PCB) and their measured metabolites are shown in Tables 3 and 4, respectively.

Sampling and analytical methods

The specific analytes and the methods for environmental sampling and analysis are described elsewhere (air, soil, and dust: Mukerjee et al. 1997b; drinking water and food: Berry et al. 1997a, 1997b). The biological methods have not been previously reported in the context of the LRGV study. Therefore, these methods are briefly described here.

Urine

Nominal 24-h urine and first-morning void samples were collected during the period of residential environmental monitoring from the primary and secondary respondent, respectively. The first-morning void was defined to include all voids collected after the last void before retiring for the night, up to and including the first void after waking up for the day. Each void was collected separately in 150 mL polyethylene containers. After collection, the respondent was asked to label each container with their identification number and the date and time of collection. The respondent was then instructed to seal the collected sample in a zip-lock bag and to place it into a provided cooler containing blue ice. Samples were stored refrigerated until they were collected at the end of the monitoring period by the field sampling team and then transported to the field monitoring staging area. At the staging location, two 10 mL aliquots were removed from the first-morning void and stabilized with nitric acid and Triton X-100 for arsenic/cadmium and mercury analysis, respectively. All samples were stored frozen at the staging location until a sufficient number of samples was available for shipping to laboratories at the Centers for Disease Control and Prevention (CDC, Division of Environmental Health Laboratory Sciences, Atlanta, GA). All samples were shipped frozen on dry ice.

In urine, arsenic, cadmium, and mercury were analyzed by Zeeman graphite furnace (Paschal et al. 1986), graphite furnace atomic absorption (Pruszkowska et al. 1983), and cold vapor atomic absorption spectroscopy (CVAAS) (Littlejohn et al. 1976), respectively. Each assay required about 2 mL of sample and each sample was analyzed in duplicate. The methods' limits of detection for each of the respective assays were 0.1, 8.0, and 0.2 μg/L, respectively.

The nonpersistent pesticides in urine were measured by capillary gas chromatography tandem mass spectrometry (GC/MS/MS) according to Hill et al. (1989) and

Table 1. Participant characteristics.

Res	Location	Subj	Relation	Occupation	Age	Sex	Wt (kg)	Ht (m)
1	Detached, single family home in residential neighborhood in western subdivision of Brownsville	P	Mother	Homemaker	51	F	68	1.63
		S	Son	Clerk and errand runner	21	M	59	1.80
2	Detached, single family home just west of Brownsville City limits	P	Mother	Migrant farmer, stays at home when living in Brownsville	45	F	61	160
		S	Daughter-in-law	Migrant farmer, stays at home when living in Brownsville	21	F	NA	NA
3*	Detached, single family home located just northeast of Brownsville City limits	P	Wife	Homemaker	34	F	72	1.57
		S	Husband	Auto mechanic, works at home	39	M	77	1.65
4*	Detached, single family home in Brownsville	P	Wife	Homemaker	30	F	63	1.63
		S	Husband	Manufacturing	30	M	63	1.73
5*	Detached, single family home located 13 miles west of Brownsville in Cameron County along Hwy 281 near town of Carricitos	P	Husband	Retired farm worker	68	M	84	1.60
		S	Wife	Retired	73	F	70	1.42
6*	Two-family duplex located 40 miles west of Brownsville in the town of Alamo	P	Mother	Misc., e.g., sells flowers, cleans offices	46	F	59	1.55
		S	Daughter	Misc., e.g., sells flowers, cleans offices	29	F	59	1.55
7*	Single family detached home located 35 miles west of Brownsville in Hidalgo County	P	Wife	Homemaker	47	F	91	1.65
		S	Husband	Tractor driver, cuts grass in irrigation ditches	47	M	82	1.70
8	Single story duplex in Brownsville	P	Mother	Homemaker	64	F	61	1.57
		S	Daughter	Homemaker	30	F	63	1.65
9*	Expanded trailer located 23 miles west of Brownsville in Hidalgo County on Hwy 281	P	Wife	Homemaker	40	F	63	1.52
		S	Husband	Farm manager	45	M	79	1.78

* Homes participating in both spring and summer phases. Conversion: 1 m = 3.281 feet; 1 kg = 2.205 pounds.

Holler et al. (1989). Samples were prepared for analysis by enzymatic hydrolysis, liquid extraction, derivatization with chloropropyl using phase-transfer catalysis, cleanup chromatography, and then concentrated. These preparatory procedures were accomplished using laboratory robotics. Samples were quantified by isotope dilution with carbon-13 labeled internal standards for all analytes. The limit of quantitation for all the nonpersistent pesticides was 1 μg/L except 3,5,6-TCP, which had a limit of 2 μg/L. Since there is no standard reference material containing the pesticide analytes of interest, a reference sample was prepared for quality assurance purposes by adding known amounts of the analyte to give concentrations in the range of interest. After spiking, the urine was sterile-filtered and dispensed into 20 mL-solvent rinsed, sterile glass Wheaton vials. These quality control samples were stored at -40°C until analysis and were

Table 2. Scope of monitoring: Number of analytes measured by pollutant class and environmental/biological medium.

Analyte class	Exposure								Body burden		
	Ingestion		Ingestion/dermal				Inhalation				
	Diet		Drinking water	House dust	Soil		Air		Blood	Breath	Urine
	Solid	Beverage			Road way	Yard	Indoor	Outdoor			
Pesticides											
Spring	225	225	50	29	NM	NM	26	26	10	NM	12
Summer	227	227	63	29	NM	NM	26	26	10	NM	12
T. elements											
Spring	8		20	44	42	42	42	42	3	NM	3
Summer	NM		NM	42	NM	NM	42	42	3	NM	3
VOCs											
Spring	NM	NM	69	NM	NM	NM	72	72	31	21	NM
Summer	NM	NM	67	NM	NM	NM	78	78	NM	NM	NM
PAHs											
Spring	13	NM	13	18	NM	NM	17	17	NM	NM	1
Summer	NM	NM	13	15	NM	NM	15	15	NM	NM	1
PCBs											
Spring	1	1	8	NM	NM	NM	NM	NM	1	NM	NM
Summer	1	1	8	NM	NM	NM	NM	NM	1	NM	NM

NM = not measured.

analyzed with each analytical run to ensure that all systems performed according to established criteria. Individual quality control charts were maintained and each analytical run met established quality control limits. The relative standard deviations for pooled quality control samples analyzed over several months were usually about 20% or less for most analytes.

1-OHPY was analyzed by modifying a method reported by Schaller et al. 1993. Samples (~50 mL) were enzymatically hydrolyzed using β-glucoronidase and centrifuged to remove suspended particulate matter. The sample was concentrated and cleaned by solid phase extraction (C18 cartridge) and elution in methanol. The sample extract was evaporated to dryness and reconstituted in methanol with pyrene external standard. This extract was analyzed using gradient high performance liquid chromatography (HPLC) with fluorescence detection (ex 336 nm; em 389 nm). The limit of detection for a 50 mL sample was 0.01 μg/L and the limit of quantitation was 0.1 μg/L. Quality control samples were prepared from sterile filtered urine spiked with 1-OHPY. The concentrations of these quality control samples, which were analyzed with each sample run, were all within expected 95% control limits. Quantitation was achieved through the use of external standards prepared in the urine matrix.

Urine creatinine was analyzed by a Kodak Ektachem 250 Dry Chemistry Analyzer™ (Kodak, Rochester, NY) using a single-slide two-point enzymatic test.

Blood

A total of about 30 mL (not including duplicate draws) was collected into color-coded vacutainers for VOCs (10 mL), persistent pesticides including PCB (15 mL), cadmium and lead (3 mL), and mercury (3 mL) analysis. Samples were collected from a single venipuncture of the antecubital vein. All vacutainers were prepared and provided by laboratories at the CDC (Division of Environmental Health Laboratory Sciences, Atlanta, GA). VOC contamination was eliminated from the vial materials.

Lead and cadmium were analyzed by graphite furnace atomic absorption spectroscopy (GFAAS) according to methods described by Miller et al. (1987) and Stoeppler and Brandt (1980), respectively. Mercury was analyzed by CVAAS method modified from Greenwood et al. (1977). The method limit of detection for each of the respective metals was 0.2, 0.6, and 0.2 μg/L.

VOC samples were stored and shipped refrigerated to laboratories at the CDC for analysis. Samples were

Table 3. Nonpersistent pesticides and their biomarkers measured in urine.

Biomarker (analyte)	Parent compound(s)	Use[1]
2-Isopropoxyphenol	Propoxur	Insecticide widely used for indoor pest control. Used both by consumers and commercial applicators.
2,5-Dichlorophenol 2,4-Dichlorophenol	1,4-Dichlorobenzene 1,3-Dichlorobenzene	Moth repellant (moth balls)
	Dichlofenthion	Nematicide, insecticide
	Prothiofos	Organophosphorous pesticide used for leaf-eating pests and for flies and mosquitoes.
	Phosdiphen	Fungicide
7-Carbofuranphenol [2,3-dihydro-2,2-dimethyl-7-hydroxybenzofuran]	Carbofuran	Carbamate insecticide and nematicide for use on soil and foliar pests.
	Benfuracarb	Carbamate insecticide and nematicide for use on seeds, soil, and foliar pests. Used on citrus crops.
	Carbosulfan	Broad spectrum carbamate insecticide, nematicide, miticide.
	Furathiocarb	Insecticide for insects in soil and for early-season pests.
2,4,6-Trichlorophenol	1,3,5-Trichlorobenzene	Herbicide
	Hexachlorobenzene	Seed protectant. By-product formed during the manufacturing of solvents and pesticides.
	Lindane	Insecticide used to treat seeds and soil for protection against cutworms and wireworms.
3,5,6-Trichloro-2-pyridinol	Chlorpyrifos	Insecticide commonly used indoors and out. Used outdoors for the control of turf insects including termites. Used indoors for household insect control, flea collars, shampoos, and spays.
	Chlorpyrifos-methyl	Insecticide used in grain storage.
4-Nitrophenol	Parathion (or Ethyl Parathion)	Restricted-use organophosphate insecticide used on farm crops especially cotton.
	Methyl Parathion	Organophosphate insecticide
	Nitrobenzene	Industrial solvent primarily used in the production of aniline but also used to produce lubricating oils.
	EPN	Acaricide, insecticide
2,4,5-Trichlorophenol	1,2,4-Trichlorobenzene	Herbicide used for aquatic weed control in irrigation canals, lakes, and ponds.
	Fenchlorphos (Ronnel)	Insecticide; no longer used in the U.S.; previously used to control indoor pests including fleas.
	Trichloronate	Insecticide
1-Naphthol	Naphthalene	Infrequently used insecticidal fumigant to control clothes moths and carpet beetles. Primarily used in the manufacture of dyes and resins. Also a product of combustion.
	Carbaryl	Broad spectrum insecticide used on residential fruits, vegetables, flowers, trees, shrubs, and lawns. Also used indoors and in collars or dust to control fleas.
2-Naphthol	Naphthalene	See above
2,4-Dichlorophenoxyacetic acid (2,4-D)	Same	Postemergent herbicide
Pentachlorophenol	Same	Wood preservative; mulluscicide

[1] Farm Chemical Handbook '96 Vol 82 Ed: RT Meister, Meister Publishing Company, Willoughby, OH, and Hayes, W.J. Pesticides Studied in Man. Williams & Wilkins, Baltimore (1982).

Table 4. Persistent pesticides and their biomarkers measured in serum.

Biomarket (analyte)	Parent compounds(s)	Use[1]
Oxychlordane	Chlordane	Widely used termiticide (80% of market) prior to being banned in April of 1988. Applied by pouring or injecting into soil around foundation.
Heptachlor epoxide	Heptachlor	Termiticide used alone or in combination with chlordane (5% of termiticide market). Also used to kill insects in seed grains and on crops. No longer in use since 1988.
trans-Nonachlor	Nonachlor	Organic compound in technical chlordane. Used as insecticide.
Beta-Hexachlorocyclohexane	Hexachlorocyclohexane (HCH)	One of eight HCH isomers (see Lindane) used as an insecticide to treat fruit, vegetable, and forest crops and as medicine to treat body lice and scabies. No longer manufactured in the U.S. (since 1977).
Dichlorodiphenyltrichloroethane (o,p'-isomer), 2,4'-DDT	Same	One of three forms making up technical DDT. Widely used pesticide for controlling crop pests and disease-carrying insects. No longer used in the U.S. but it is used in other countries throughout the world.
Dichlorodiphenyldichloroethylene (p,p'-isomer), 4,4'-DDE	4,4'-DDT	Environmental or biological conversion product of 4,4'-DDT
Gamma-Hexachlorocyclohexane (Lindane)	Same	Insecticide used to treat fruit, vegetable, and forest crops and as medicine to treat body lice and scabies. No longer manufactured in the U.S. (since 1977).
Hexachlorobenzene	Same	Fungicide used as a seed protectant. Also found as an industrial waste.
Polychlorinated biphenyls as Aroclor 1260	Same	Widely used insecticide from 1940 to early 1970s for control of household, garden, ornamental, and public health pests. Also used as coolant and lubricant in transformers and other electrical equipment. Production in U.S. stopped in 1977.

[1] Farm Chemical Handbook '96 Vol 82 Ed: RT Meister, Meister Publishing Company, Willoughby, OH, and Hayes, W.J. Pesticides Studied in Man. Williams & Wilkins, Baltimore (1982).

analyzed by purge and trap gas chromatography using isotope dilution and full scan high resolution mass spectrum detection according to Ashley et al. (1992). Each sample was spiked with a labeled stable isotope for each of the analytes of interest. Samples were heated (35°C) and helium purged for 15 min and then trapped on Tenax™. Adsorbed water was removed from the Tenax by drying with helium for 6 min. The trap was then thermally desorbed at 180°C for 4 min and the VOCs were cryogenically trapped at the GC injection port. The cryogenic trap was then heated and the VOCs were separated by a DB-624 capillary column before high resolution mass spectrum detection (full scan, 40-200 amu, 1 scan/s). Quantitation was accomplished from specific ion responses of the unknown sample relative to those of the isotopically labeled analogs based on a six-point calibration curve. Laboratory blanks were prepared from a water source shown to be absent of VOCs. No reference materials exist for VOCs in blood. Therefore, accuracy was assessed based on the analysis of sample spikes. The method limit of detection for most analytes ranged from 0.01 to 0.04 μg/L. More specific information can be found in Ashley et al. (1992).

Persistent pesticides and chlorinated compounds were analyzed in blood serum according to previously published methods (Burse et al. 1990a; 1990b). Serum was separated from the whole blood sample by allowing the sample to clot (<30 min) and then centrifugation (1500 x g for 15 min). The serum (>5 mL) was transferred by pipette to a Wheaton bottle and crimp-sealed with Teflon lined caps. The serum sample was stored and shipped frozen (-20°C) to the CDC laboratories. After denaturation with methanol, samples were extracted with hexane and ethyl ether (one to one). The extracts were eluted through a micro florisil column using 6% ethyl ether/petroleum ether and 15% ethyl ether/petroleum ether. The 6% fraction was

further treated with sulfuric acid and eluted through a micro column of silica gel (deactivated with 5% water) from which two fractions (hexane and benzene) were obtained. All three fractions were analyzed using electron capture (^{63}Ni) gas liquid chromatography with packed columns composed of SP-2250/SP-2401 or SE-30. Analytes were analyzed using an internal standard approach, relative response factors, and analytical standards at four concentrations. The method limits of detection ranged from 0.1 to 1.0 μg/L for the various analytes. Quality assurance procedures for this analysis included the use of matrix blanks and spikes (calf serum), and duplicate sample analysis.

Breath

Samples were collected immediately after the blood sample collection from the primary participant only using an established simple and compact sampling system designed for the collection of alveolar breath for subsequent VOC analysis (Raymer et al. 1990; Thomas et al. 1991). The protocol for alveolar breath sampling included the subject breathing through one-way valves such that inhalations were purified through an activated charcoal filter and exhalations passed into a 1.27 i.d. x 762 cm Teflon™ tube. The sample was collected after four respirations in order to clear the sampler tubing and the subject's airways of ambient VOCs. The sample was drawn from the front-end of the Teflon™ tube through a critical orifice into 1.8 L Summa™ polished canisters over an 80-s period. This method has been shown to capture 97% alveolar breath. The entire breath sampling procedure required approximately 2 min. The canister sample was stored, shipped, and kept at room temperature until analysis. Collection of VOCs in passivated Summa™ canisters has previously been shown to be quantitative for both air and breath samples (Jayanty et al. 1992; Lindstrom and Pleil 1996). Analysis was accomplished by pulling a 50 mL aliquot of the breath from the canister through a nafion dryer (Perma-Pure Products, Toms River, NJ) and into a cryogenic trap at the inlet of the gas chromatograph (Varian 1400, Varian Associates, Palo Alto, CA) in line with an LKB 2091 mass spectrometer (LBK, Bromma, Sweeden) operated in selected ion mode. Quantification was accomplished using response factors from the dynamic dilution of a primary standard containing all of the target analytes. Standards including d_6-benzene, perfluorobenzene, and perfluorotoluene were spiked onto the cryofocusing trap at the time of analysis. Quality control samples included two duplicates, two field controls, and one field blank. The method's limit of detection ranged from 2.5 μg/m^3 for vinylidene chloride to 3.5 μg/m^3 for para-dichlorobenzene.

Questionnaires

Five different questionnaires (available in English or Spanish) were employed to complement the environmental and biological monitoring including: 1) a Pre-monitoring Survey to characterize the residence's location, physical layout, and household characteristics (e.g., type of heating and cooking); 2) a Post-monitoring Activity Pattern Questionnaire to obtain information about the participant's location and activities (e.g., time indoors, outdoors, in car); 3) a 24-h Food Diary to obtain information about the foods eaten during the collection period; 4) a Meal Selection and Supplemental Information Questionnaire to gauge the representativeness of the 24-h collected diet to the subject's typical diet; and 5) a Food Group Checklist to classify the collected diet into simple food groups. These questionnaires were administered by a trained bilingual interviewer who was local to the study region.

Statistical comparisons

Interpretation of the current study's biological results is based on individual and group comparisons with data from the CDC's National Center for Health Statistics collected as a part of the NHANES II and III. In addition to these inter-study comparisons, differences between the spring and summer results were also evaluated. A summary of the different types of comparisons made are shown in Table 5.

Difference between seasons

The spring to summer seasonal difference in biomarker levels was evaluated by testing various null hypotheses as appropriate. For the nonpersistent pesticides, a one-sided test was used (i.e., H_o: $Conc._{Spr} > Conc._{Sum}$) since it was *a priori* believed that pesticide exposure would be higher in the summer due to its increased application and use in the summer. However, for the persistent pesticides, metals, and 1-OHPY, a two-sided test (i.e., H_o: $Conc._{Spr} = Conc._{Sum}$) was appropriate since the authors had no preconceived notion of their seasonal trend. In each case, the criteria for significance was set at $p \leq 0.10$. Multiple comparisons were taken into account using the conservative approach of the Bonferroni interval (α/k) where α is the sgnificance

Table 5. Summary of seasonal and NHANES comparisons.

Pollutant class (medium)	Comparison		Table ref.
	Season	Reference	
Nonpersistent pesticides (urine)	H_o: spring-summer>0	NHANES III - Statistical test based on the percentage of samples with concentrations above the limit of detection (%detect) - Descriptive based on median and maximum values	6
Persistent pesticides (serum)	H_o: spring-summer=0	NHANES II - Descriptive based on median and maximum values	7
Metals and PAHs (urine)	H_o: spring-summer=0	NHANES reference not available	8
Metals (blood)	H_o: spring-summer=0	NHANES III (Pb only) - Statistical test based on %detect - Descriptive based on median and maximum values	8
VOCs (blood)	Not possible (only one season sampled)	NHANES III - Statistical test based on %detect - Descriptive based on median and maximum values	9

level and k is the number of comparisons (Rosner 1995). For the urinary measurements, k=12, 3, and 1 for the pesticides, metals, and PAHs, respectively. For the blood measurements, k=10 and 3 for the persistent pesticides (including PCB) and metals, respectively. Because the difference between two paired measurements that were below the limit of detection was not discriminating in this evaluation, a criteria was established that there be at least six data pairs where at least one measurement was above the limit of detection over the two seasons in order for the analyte to be included in this statistical analysis. Seasonal differences were evaluated nonparametrically by applying the Wilcoxon sign rank test (Rosner 1995) to the difference of the subject paired spring and summer values as shown in Eq. 1.

$$SD_{ijk} = Spr_{ijk} - Smr_{ijk} \quad (1)$$

where,

SD_{ijk} = the difference between spring and summer for person *i*, media *j*, and analyte *k*;

Spr_{ijk} = the concentration of analyte *k* in media *j* and person *i* measured in the spring study phase; and

Smr_{ijk} = the concentration of analyte *k* in media *j* and person *i* measured in the summer study phase.

Differences in urine measurements were based on creatinine corrected values to minimize the confounding influence of hydration. When one of the two values was below the method's limit of detection, then a value of ½ the detection limit was assigned.

Comparison with NHANES III

Methods for sampling and analysis of the nonpersistent pesticides in urine and VOCs in blood were essentially the same between the current study and NHANES III so that direct comparisons could be made between these data sets. The analytical labs and methods were identical, however, there were three important differences in sampling strategy: 1) LRGV sampled two individuals from each home whereas NHANES III sampled a single individual per household; 2) LRGV included longitudinal sampling such that the same individual was sampled over two seasons whereas NHANES included only a single sample from each individual; and 3) NHANES III sampled individuals year-round whereas the current study was conducted during discrete periods of time within each of two seasons. The interaction effect due to 1 and 2 was

evaluated for each analyte using the SAS General Linear Models Procedure.

Differences between the two studies with respect to nonpersistent pesticides in urine and VOCs in blood were made based on a comparison of the proportion of samples above the method's limit of detection. This approach was used rather than more direct comparisons (e.g., difference between means) since the proportion of measurements above the limit of detection was low for both studies (median of 0.45 and 0.35 for pesticides, and 0.13 and 0.13 for VOCs for NHANES III and LRGV, respectively), and because limited information was available on the distribution of the NHANES III data. Additional descriptive comparisons were made with the NHANES median and 95th percentiles for each season. As a conservative comparison, the 95th percentile from NHANES III was compared to the mean of the highest two measured values (max_2) from LRGV.

The cumulative binomial distribution was used to test for differences in the proportion of samples above the method limit of detection between NHANES III and LRGV (Eq. 2). NHANES III established the proportion of samples expected to be above the method limit of detection for a national reference population. The LRGV subsample for the spring season was compared to this "true" proportion:

$$P(X \le x|n,p) = \sum_{x}^{x} \binom{n}{x} p^{x} q^{n-x} \qquad (2)$$

where,
n = the number of LRGV individuals sampled;
x = the number of LRGV samples above the method limit of detection;
p = the true population proportion of measurements above the limit of detection given by NHANES III; and
q = the true population proportion of measurements below the limit of detection given by NHANES III.

Intrapersonal seasonal variability

Twelve individuals were sampled over two seasons in order to investigate within person seasonal variability in biomarker levels of pesticides, metals, and PAHs. This source of variability was analyzed by regressing the spring results on the summer values for blood and urine. For the urine analytes, the creatinine corrected results were used. For all analytes, when a result was below the method limit of detection, a value of one-half the detection limit was ascribed. Because the data appeared to be skewed to the right reflecting a log-normal distribution (and, in fact, tested non-normal using the Shapiro-Wilk statistic), the regressions were conducted on the Logarithms of the data.

$$Log(Smr) = b_0 + b_1(Log(Spr)) \qquad (3)$$

where,
Smr = the summertime biomarker concentration in blood (μg/L) or urine (μg/g Creatinine) for person i;
Spr = the springtime biomarker concentration in blood (μg/L) or urine (μg/g Creatinine) for person i;
b_0 = the y intercept of the line given by least squares fit; and
b_1 = the slope of the line given by least squares fit.

In most cases the Log values were found to be normally distributed (Shapiro-Wilk statistic, $p \le 0.05$). In those cases when the transformed data were also non-normal (Shapiro-Wilk statistic, $p \le 0.05$), the two seasons were compared by rank using Spearman correlation. For three nonpersistent pesticides and another three persistent pesticides, regression analysis was not meaningful because there were not at least two measurements in a season above the limit of detection.

Regression analysis was also used to evaluate the relationship between chlorpyrifos air and dust levels (Eq. 4) and between these environmental media and the 3,5,6-TCP biomarker levels in urine (Eq. 5). Again, due to the right-skewed distribution of the environmental concentration measurements, these values were Log transformed.

$$Log(IA) = b_0 + b_1(Log(HD)) \qquad (4)$$

$$3,5,6\text{-}TCP = b_0 + b_1(Log(EC)) \qquad (5)$$

where,
IA = the indoor air concentration ($\mu g/m^3$);
HD = the house dust concentration (μg/g);
3,5,6-TCP = the concentration of the chlorpyrifos metabolite in urine (μg/g creatinine);
EC = the environmental concentration of chlorpyrifos in indoor air or house dust; and
b_0 and b_1 are defined as above.

RESULTS

The analytes and summary results (percent above the method limit of detection, median, and maximum) by season are shown in Tables 6, 7, 8, and 9 for the measurement of persistent pesticides (including PCB), nonpersitent pesticides, metals (including PAH), and VOCs in their respective biological medium. These results are presented with an analysis of seasonal differences and in comparison to NHANES reference results.

Statistical analyses including regression, univariate procedures, and Shapiro-Wilk "W" statistic for normality were conducted using SAS™ 6.01 (SAS Institute Inc., Cary, NC).

Extensive quality assurance procedures were implemented in order to assure data validity. Laboratory procedures included duplicate sample analysis for persistent pesticides in blood serum (n=3) and VOCs (n=2) and lead (n=3) in whole blood. The median (and range) coefficient of variation (CV) for each of these respective analyte groups was 4.5% (0%-12%), 21% (1%-65%), and 5.0% (4%-6%). This level of variability is consistent with the reported precision of the methods (Burse et al. 1990a, 1990c; Ashley et al. 1992; Miller et al. 1987). In addition, each metal analysis (blood and urine) was conducted in duplicate. The analysis of cadmium in blood and urine were characterized by a CV≤5% whereas mercury in blood and urine and lead and cadmium in blood had a CV of ~10%. All laboratory results were verified through an EPA audit procedure before being finalized in the U.S. EPA Final Report to the Community (1994).

Difference between seasons

Seasonal differences were evaluated for nonpersistent pesticides, metals, and 1-OHPY in urine, and persistent pesticides and lead in blood. Seasonal differences in blood VOCs, cadmium, and mercury could not be evaluated since these measurements were only made in the spring.

In urine (creatinine corrected), there were 7 of 12 nonpersistent pesticides, 3 of 3 metals, and 1 of 1 PAH measured in a sufficient number of paired samples (i.e., ≥6) between the two seasons where at least one of the values was above the limit of quantification. The Wilcoxon sign rank test revealed that for two of seven nonpersistent pesticides measured in urine (2,5-dichlorophenol, and 3,5,6-TCP), there was a significant difference ($p \leq 0.10$, a one-sided test, k=12) between seasons, with the summer values being greater than spring (Table 6). Similarly, for three of three metals (As, Cd, Hg) and the pyrene metabolite, 1-OHPY, a significant seasonal difference was detected ($p \leq 0.10$, two-sided test, k=3 and 1, respectively) again with the summer values greater than the spring in each case (Table 7). The seasonal descriptive statistics were consistent with this analysis. Summer median and maximum values were always greater than in the spring. Of the metals monitored in blood, only lead results were available for both seasons and no statistically significant seasonal difference was detected.

For the persistent pesticides and chlorinated compounds in blood serum, a seasonal effect could be evaluated for 5 of 10 analytes where there were a sufficient number of measurements above the method limit of detection between the two seasons (again a criteria of at least six data pairs where one measurement was above detection was applied). A significant ($p \leq 0.10$, two-sided, k=10) difference was observed for hexachlorobenzene with summer levels being greater than spring (Table 8).

Mercury was measured both in urine and in blood during the spring phase. The relationship between the concentrations in the two media was investigated by regression analysis. Using the creatinine corrected urine values, and assigning ½ the detection limit to the four blood measurements below the limit of detection, the regression on the log transformed data was significant (R^2=0.31, n=18, p=0.016) yielding an intercept of 0.49 (SE=0.37, p=0.20) and a slope of 0.96 (SE=0.36, p=0.016).

Comparison with NHANES III

The effect of sampling from within the same household (within home) and over two seasons (season) was evaluated using SAS's General Linear Models (GLM) procedure. This analysis showed that both of these interactions were significant ($p \leq 0.05$, uncorrected for multiple comparisons) for 4-nitrophenol, while only the "within-home" was significant for 2,4-D. In addition, both interaction effects were found for 2,4-dichlorophenol, 3,5,6-TCP, while season alone was significant for pentachlorophenol and 2,4-dichlorophenol. Interpretations about the meaning of differences between LRGV and reference levels are made cautiously due to these interactions which are not present in the NHANES reported data.

In addition to the seasonal comparison, Table 6 also provides a comparison of the LRGV nonpersistent pesticide biomonitoring results with NHANES III

Table 6. Nonpersistent pesticide results, seasonal differences, and comparison with NHANES III reference data.

Analyte	%detects[1]	Comparison		Med[4] (μg/L)	Max[5] (μg/L)
		Season[2]	NHANES[3]		
2-Isopropoxyphenol					
Spring	1/17 (6%)	n=0	NS	<MLD	1.1
Summer	0/12 (0%)	IN	NS	<MLD	<MLD
NHANES III	6.8%			<MLD	1.7
2,5-Dichlorophenol					
Spring	17/17 (100%)	**n=11**	NS	12	92 (84)
Summer	12/12 (100%)	*	NS	**60**	240 (225)
NHANES III	98%			30	790
2,4-Dichlorophenol					
Spring	8/17 (47%)	n=11	NS	<MLD	3.3 (3.2)
Summer	10/12 (83%)	NS	NS	**3.0**	6.8 (6.2)
NHANES III	64%			2.2	64
7-Carbofuranphenol					
Spring	0/17 (0%)	n=0	NS	<MLD	<MLD
Summer	0/12 (0%)	IN	NS	<MLD	<MLD
NHANES III	1.5%			<MLD	<MLD
2,4,6-Trichlorophenol					
Spring	1/17 (6%)	n=1	NS	<MLD	2.2
Summer	0/12 (0%)	IN	NS	<MLD	<MLD
NHANES III	9.5%			<MLD	3.3
3,5,6-Trichloro-2-pyridinol					
Spring	13/17 (77%)	**n=11**	NS	1.9	6.4 (5.6)
Summer	11/12 (92%)	**	NS	**3.2**	11 (9.7)
NHANES III	82%			3.0	13
4-Nitrophenol					
Spring	12/17 (71%)	n=11	NS	1.4	**5.5** (4.4)
Summer	12/12 (100%)	NS	*	2.7	**13 (11)**
NHANES III	41%			<MLD	5.2
2,4,5-Trichlorophenol					
Spring	7/17 (41%)	n=5	NS	<MLD	**4.2 (3.7)**
Summer	1/10 (10%)	IN	NS	<MLD	1.3
NHANES III	20%			<MLD	3.0
1-Naphthol					
Spring	16/17 (94%)	n=11	NS	2.8	38 (27)
Summer	11/11 (100%)	NS	NS	2.8	22 (18)
NHANES III	86%			4.4	43
2-Naphthol					
Spring	16/17 (94%)	n=11	NS	2.6	**38** (27)
Summer	12/12 (100%)	NS	NS	2.6	11 (10)
NHANES III	81%			3.4	30

(Table Continued.)

Table 6. Continued.

2,4-D					
Spring	5/17 (29%)	n=4	*	<MLD	**2.8 (2.2)**
Summer	4/12 (33%)	IN	*	<MLD	1.6 (1.6)
NHANES III	12%			<MLD	1.8
Pentachlorophenol					
Spring	5/17 (29%)	n=8	NS	<MLD	3.2 (2.4)
Summer	8/12 (67%)	NS	NS	1.0	7 (5.2)
NHANES III	64%			1.5	8.2

[1] Percentage of samples measured above the limit of detection.
[2] The significance of LRGV seasonal differences are evaluated based on the difference between seasons using the Wilcoxon signed rank test (one-sided; H_0: spring > summer) correcting for multiple comparisons (k=12) using the Bonferroni interval. The evaluation is based on "n" data pairs where at least one value was above the limit of detection for the 12 individuals sampled in both seasons.
[3] Differences with NHANES III are evaluated by testing H_0 that the proportion detected in NHANES III (Hill et al. 1995) equals the proportion detected in LRGV during the spring and summer.
[4] Median value that includes measurements below the limit of detection. LRGV values exceeding NHANES III are bolded.
[5] Maximum value: for NHANES III the 95th percentile is reported; for LRGV, the maximum value is shown with the mean of the highest two values shown in ( ). LRGV values exceeding NHANES III are bolded.
* Indicates significance at the 0.10 level.
** Indicates significance at the 0.05 level.
IN = insufficient number of valid data pairs (i.e., <6) in order to evaluate the comparison.
NS = not significant.
<MLD = less than the method limit of detection.

reference data. The proportion of samples above the limit of detection from the current study was significantly greater ($p \leq 0.10$; two-sided, k=12) than what was expected from NHANES III for 2 of 12 non-persistent pesticides: 4-nitrophenol and 2,4-D. Further evidence of elevated biomarker levels for the LRGV sample for these analytes relative to the NHANES III reference was given by higher median and max_2 values. No other LRGV median or max_2 values exceeded NHANES III except for that of 2,4,5-trichlorophenol which had a max_2 of 3.7 μg/L exceeding the NHANES III 95th percentile value of 3.0 μg/L.

Persistent pesticides and PCB

Only NHANES II data were available for this comparison. Because these results were generated from laboratories using different methods with different sensitivities, LRGV results are only descriptively compared to the NHANES II median and 95th percentile values as shown in Table 8. However, in most cases, the NHANES II comparison values are below the limit of detection so that even a descriptive comparison is not possible. Of the four analytes for which NHANES reported values above the limit of detection, LRGV exceeded the median and/or 95th percentile in three cases, i.e., 4,4'-DDE (transformation product of DDT), trans-nonachlor, and PCBs as Aroclor 1260.

As shown in Table 8, 4,4'-DDE was above the limit of detection in all 28 samples for which there were reportable results, whereas the parent (4,4'-DDT) and the contaminant isomer (2,4'-DDT) were only above the limit of detection in 5 of 28 and 0 of 28 cases, respectively. For the five cases where both the parent (4,4'-DDT) and metabolite (4,4'-DDE) were above the method limit of detection, the values were correlated (R^2=0.88; p=0.065) when one outlying data pair (spring, HID 001, primary respondent) was removed. With this point removed, the regression yielded a slope of 157 (SE=42) and intercept of -99 (SE=20). The ratio of 4,4'-DDE to 4,4'-DDT ranged from 6 to 87 with a median value of 33. Although the 4,4'-DDE analytes were measurable in environmental media (indoor air-13/15, outdoor air-12/15, house dust-12/15, and diet-3/15), no significant environmental correlations (Spearman or Pearson; $p \leq 0.10$) were detected for it or for 2,4'-DDE (measured in diet only), 2,4'-DDT (measured in diet only), or 4,4'-DDT (measured in air,

Table 7. Metals in blood and 1-hydroxypyrene in urine results, seasonal differences, and comparison with NHANES III reference data.

Analyte		%detects[1]	Comparison		Med[4] (μ/L)	Max[5] (μ/L)
			Season[2]	NHANES III[3]		
Metals (urine)						
As	Spring	11/18 (61%)	**n=12** **	NA	8.0	41 (34)
As	Summer	12/12 (100%)		NA	27.2	427.4 (255)
Cd	Spring	12/18 (66%)	**n=12** **	NA	0.2	0.8 (0.075)
Cd	Summer	12/12 (100%)		NA	**1.0**	2.3 (1.89)
Cd	NHANES III	NA	NA	NA	0.53	2.41
Hg	Spring	18/18 (100%)	**n=12** **	NA	0.7	6.9 (4.5)
Hg	Summer	12/12 (100%)		NA	2.9	8.6 (7.6)
Metals (blood-whole)						
Pb	Spring	16/16 (100%)	n=12 NS	NS	3.1	6.4 (6.4)
Pb	Summer	12/12 (100%)		NS	3.6	8.0 (7.0)
Pb	NHANES III	98%	NA	NA	3.5	12.7
Hg	Spring	14/18 (78%)	NA	NS	1.3	7.3 (5.6)
Cd	Spring	8/16 (50%)	NA	NA	<MLD	0.5 (0.5)
PAH (1-Hydroxypyrene)						
	Spring	10/17 (59%)	**n=12** **	NA	0.1	2.4 (1.02)
	Summer	11/12 (92%)		NA	0.5	2.7 (2.15)

[1] Percentage of samples measured above the limit of detection.
[2] The significance of LRGV seasonal differences are evaluated based on the difference between seasons using the Wilcoxon signed rank test (two-sided; H_0: spring = summer) correcting for multiple comparisons using the Bonferroni interval. The evaluation is based on "n" data pairs where at least one value was above the limit of detection for the 12 individuals sampled in both seasons.
[3] Differences with NHANES III are evaluated by testing H_0 that the proportion detected in NHANES III equals the proportion detected in LRGV during the spring and summer.
[4] Median value that includes measurements below the limit of detection. LRGV values exceeding NHANES III are bolded.
[5] Maximum value: for NHANES III the 95th percentile is reported; for LRGV, the maximum value is shown with the mean of the highest two values shown in ( ). LRGV values exceeding NHANES III are bolded.
* Indicates significance at the 0.10 level.
** Indicates significance at the 0.05 level.
IN = insufficient number of valid data pairs (i.e., <6) in order to evaluate the comparison.
NS = not significant.
NA = data not available.
<MLD = less than the method limit of detection.

diet, dust, and drinking water). Although there were only a few measurements above the limit of detection, blood 4,4'-DDT (n=5) was compared to environmental levels in dust (n=4), indoor air (n=4), and outdoor air (n=2). As with 4,4'-DDE, no significant environmental correlates were observed suggesting that the environmental measurements did not capture the biomarker relevant exposure likely due to the limited time scale of the environmental monitoring relative to the half-life of the biomarker.

The trans-nonachlor max_2 exceeded the NHANES II 95th percentile during both the spring and summer study phases. The highest spring value was measured for the secondary subject in home 4 (3.49 μg/L) while both subjects in home 5 also exceeded the 95th percentile although with lesser values (1.78 and 1.70 μg/L). During the summer, blood levels for both subjects in home 5 again were elevated (2.03 and 1.21 μg/L) while the previously measured high value for home 4 dropped to 0.24 μg/L. As was the case for DDE,

Table 8. Persistent pesticides in blood serum, difference between seasons, and comparison to NHANES II[1] reference values.

Analyte	%detects[2]	Med[3]	Max[4]	Season[5]
Dichlorodiphenyldichloroethylene (p,p'-isomer), 4,4'-DDE				
Spring	16/16 (100%)	**17.9**	**137 (92.7)**	n=11
Summer	12/12 (100%)	**21.3**	**109 (92.4)**	NS
NHANES II	NA	12.6	52.9	NA
Trans-onachlor				
Spring	13/16 (81%)	0.59	**3.49 (2.60)**	n=10
Summer	11/12 (92%)	0.45	**2.03 (1.62)**	NS
NHANES II	NA	<QL	1.2	NA
Heptachlor epoxide				
Spring	12/16 (75%)	0.27	0.84 (0.76)	n=9
Summer	6/12 (50%)	0.250	1.05 (0.70)	NS
NHANES II	NA	<QL	<QL	NA
Beta-Hexachlorocyclohexane				
Spring	11/16 (69%)	0.73	1.88 (1.65)	n=9
Summer	7/12 (58%)	0.71	1.43 (1.21)	NS
NHANES II	NA	<QL	<QL	NA
Hexachlorobenzene				
Spring	3/16 (19%)	<MLD	0.19 (0.16)	**n=11**
Summer	12/12 (100%)	0.095	0.30 (0.23)	**
NHANES II	NA	<QL	1.2	NA
Oxychlordane				
Spring	6/16 (38%)	<MLD	1.32 (0.88)	n=5
Summer	5/12 (42%)	<MLD	0.55 (0.49)	IN
NHANES II	NA	<MLD	<MLD	NA
Polychlorinated biphenyls (PCB) as Aroclor 1260				
Spring	6/16 (38%)	<MLD	**99.3 (85.8)**	n=5
Summer	5/12 (42%)	<MLD	**99.4 (96.4)**	IN
NHANES II	NA	4.2	30	NA
Dichlorodiphenyltrichloroethane (o,p'-isomer), 4,4'-DDT				
Spring	3/16 (19%)	<MLD	2.28 (1.63)	n=2
Summer	2/12 (17%)	<MLD	1.25 (1.17)	IN
NHANES II	NA	<MLD	<QL	NA
Gamma-Hexachlorocyclohexane				
Spring	2/16 (13%)	<MLD	0.24 (0.22)	n=1
Summer	0/12 (0%)	<MLD	<MLD	IN
NHANES II	NA	<MLD	<MLD	NA
Dichlorodiphenyltrichloroethane (p,p'-isomer), 2,4'-DDT				
Spring	0/16 (0%)	<MLD	<MLD	n=0
Summer	0/12 (0%)	<MLD	<MLD	IN
NHANES II	NA	<QL	2.7	NA

Table 8. Continued.

[1] NHANES II results are based on blood serum samples from 7265 individuals during the period from 1976 to 1980. Median and 95th percentile results were obtained from a reanalysis of the data from Murphy and Harvey (1985) to include measurements below detection as reported in U.S. EPA (1994). The NHANES II and LRGV frequencies of detection are not compared since the NHANES II method sensitivity differs substantively from that of the current study.
[2] Number and percentage of samples measured above the limit of detection.
[3] Median value includes samples that were measured below the limit of detection.
[4] Maximum value. The NHANES II 95th percentile is compared to the LRGV maximum value. The mean of the two highest LRGV values is shown in ( ) as a conservative comparison. LRGV values exceeding NHANES II are bolded.
[5] The significance of LRGV seasonal differences are evaluated based on the difference between seasons using the Wilcoxon signed rank test (two-sided; H_0: summer = spring) correcting for multiple comparisons (k=10) using the Bonferroni interval. The evaluation is based on "n" data pairs where at least one value was above the limit of detection for the 12 individuals sampled in both seasons.
* Indicates significance at the 0.10 level.
** Indicates significance at the 0.05 level.
ND = not detected.
IN = insufficient number of valid data pairs (i.e., <6) in order to evaluate the comparison.
<QL = less than the limit of quantification.

trans-nonachlor was either not measured (air, house dust, and soil) or was below the limit of detection (diet and drinking water) in environmental media so that exposure pathways could not be delineated.

The LRGV max_2 for PCBs as Aroclor 1260 exceeded the NHANES II 95th percentile due to high levels measured in both the primary (99 and 93 μg/L) and secondary (72 and 99 μg/L) subjects of HID 7 in the spring and summer, respectively. All of the other participants that were sampled measured below the NHANES II median value of 4.2 μg/L. PCBs were either not measured (soil, air, and dust) or were below the limit of detection (drinking water and diet) in environmental media so that correlates were not identifiable (Berry et al. 1997a, 1997b; Mukerjee et al. 1997b). However, for this particular house, based on the pre-monitoring questionnaire, it was disclosed that residents caught and ate carp from a nearby irrigation ditch. Although the fish was not a part of the household's 24-h diet sample, the sampling team requested a portion of the raw fish from the household freezer. This fish was found to have high levels of PCBs (399 mg/kg) and it is the likely source for the high blood serum values for the primary and secondary subject in this household (Berry et al. 1997b).

VOCs in blood

Measurements were only made in the spring study phase. For the VOCs with at least one measurement above detection, results relative to NHANES III are presented in Table 9. VOCs with no samples above the limit of detection included 1,1,2,-trichloroethane, 1,1,2,2-tetrachloroethane, 1,1-dichloroethene, 1,2-dichlorobenzene, 1,2-dichloroethane, 1,2-dichloropropane, 1,3-dichlorobenzene, chlorobenzene, dibromomethane, dichloromethane, trichloroethene, and cis-1,2-dichloroethene. This low rate of detection is consistent with Ashley et al. (1994) who reports a detection rate of <10% for these same analytes. Based on the percentage of measurements above the limit of detection, blood VOC levels were significantly ($p \leq 0.10$; two-sided; k=31) elevated for two compounds, dibromochloromethane and carbon tetrachloride (CCl_4). In contrast, ethylbenzene, styrene, 1,4-dichlorobenzene, and tetrachloroethene were significantly less than the NHANES III reference.

Levels of dibromochloromethane and carbon tetrachloride in blood were compared to measured concentrations in air and drinking water in order to identify possible pathways of exposure. Dibromochloromethane was not detected in any of the indoor or outdoor air samples, although it was detected in the drinking water in eight of nine and five of six homes in the spring and summer, respectively (Berry et al. 1997a). There were no significant ($p \leq 0.10$) correlations (Pearson or Spearman) with the water concentrations suggesting that some other nonresidential source may have been contributing to the measured biomarker levels.

Carbon tetra-chloride was above the limit of detection in the blood of the primary subject in HID 2 (0.029 μg/L) and the secondary subject in HID 6

Table 9. Spring phase blood VOC results in comparison to NHANES III.

VOC	LRGVES (spring) (n=16) %detect[1]	Med[2] (μg/L)	Max[3] (μg/L)	Comp[4]	NHANES III[5] (n=1100) %detect	Med (μg/L)	95%ile (μg/L)
2-Butanone	16/16 (100%)	**5.9**	**18**	NS	99.7	5.4	16.9
Acetone	16/16 (100%)	1555	5210	NS	99.7	1800	>6000
Benzene#	16/16 (100%)	**0.12**	0.21	NS	91.2	0.06	0.48
m-Xylene and p-Xylene#	15/16 (94%)	0.19	0.65	NS	99.7	0.19	0.78
o-Xylene#	15/16 (94%)	**0.12**	0.34	NS	96.4	0.11	0.3
Toluene#	13/16 (81%)	0.17	0.7	NS	99.2	0.28	1.5
Ethylbenzene#	11/16 (69%)	0.04	0.18	-/*	94.4	0.06	0.25
1,1,1-Trichloroethane	9/16 (56%)	**0.16**	0.43	NS	76.2	0.13	0.80
Chloroform#	8/16 (50%)	0.02	0.04	NS	58.0	0.02	0.13
Styrene#	8/16 (50%)	0.02	0.06	-*	87.9	0.04	0.18
1,4-Dichlorobenzene#	7/16 (44%)	ND	1.7	-/*	94.6	0.33	9.2
Dibromochloromethane	6/16 (38%)	ND	**0.05**	NS	14.5	NA	0.024
Tetrachloroethene#	4/16 (25%)	ND	0.59	-/*	74.9	0.06	0.62
Bromodichloromethane	3/16 (19%)	ND	0.02	NS	16.5	NA	NA
Bromoform	3/16 (19%)	ND	0.07	NS	9.9	NA	0.034
Carbon Tetrachloride#	2/16 (13%)	ND	0.03	+/*	1.4	ND	0.061
1,1-Dichloroethane	1/16 (6%)	ND	0.01	NS	4.6	NA	ND
Hexachloroethane	1/16 (6%)	ND	0.14	NS	1.1	NA	0.038
trans-1,2-Dichloroethene#	1/16 (6%)	ND	0.03	NS	2.7	NA	ND

[1] Percentage of samples measured above the limit of detection. Of the 18 subjects participating, blood collections were not possible for the 2 secondary subjects in homes 5 and 8.
[2] Median value including measurements that were below the limit of detection. Values exceeding NHANES III are shown in bold.
[3] Maximum value as the average of two highest values (when only one value is reported, i.e., n=1, then that value is listed). Values exceeding NHANES are shown in bold.
[4] Comparisons with NHANES III are evaluated by testing H_0 that the proportion detected in NHANES III equals (two-sided test) the proportion detected in LRGV (spring only). Multiple comparisons are adjusted for using the Bonferroni interval where k=31 is the number of comparisons. "+/-" indicates whether the percent detect was greater (+) or less than (-) expected from NHANES III. VOCs with a frequency of detection significantly > NHANES III are shown in bold.
[5] NHANES III comparison results including percent of measurements above detection, median, and 95th percentile values are from Ashley et al. (1995).
* Indicates significance at the 0.10 level.
# VOCs also measurable in breath.

(0.020 μg/L). Although CCl_4 was undetectable in all of the water samples, it was at measurable concentrations in all of the indoor and outdoor air samples. Extremely little variation in indoor or outdoor CCl_4 air levels was observed (mean (±std) indoor: 0.681 (0.012) μg/m^3; outdoor: 0.684 (0.010) μg/m^3). The peak outdoor air concentration of 0.705 μg/m^3 was measured in home 6 where the secondary subject was one of two subjects measured above the limit of detection. A comparison of descriptive statistics revealed that the LRGV max_2 exceeded the NHANES III 95th percentile in two cases: 2-butanone (24.0 μg/L for the primary subject in home 1) and dibromochloromethane (0.054 μg/L for the primary subject in home 8). Similarly, the LRGV median was high relative to NHANES III for benzene, o-xylene, and 1,1,1-trichloroethane.

There were only a few breath measurements that were above the method limit of detection. Of the 21 analytes measured across 9 individuals (spring primary participants), only 5 samples were above detection yielding a detection rate of <3%. Because of this low rate of detection, there was only one analyte (i.e., toluene) above detection in two individuals that was common to breath and blood. For these two samples, the two measurements did not correspond. According to the blood measurements, the highest concentrations were found in HID 9 (0.50 μg/L) and 6 (0.29 μg/L) whereas breath concentrations were only detectable in HIDs 1 (2.6 $\mu g/m^3$) and 4 (4.0 $\mu g/m^3$). The other VOC breath measurements that were above the limit of detection included tetrachloroethylene (n=1; 7.9 ng/L in home 9); 1,1,1-trichloroethylene (n=2; maximum value of 35.2 ng/L in home 9). VOCs measured in breath but not in blood included methylene chloride, vinylidene chloride, and 1,1,1-trichloroethylene.

Intrapersonal seasonal variability

Regression analysis showed a significant correlation ($p \leq 0.05$) between spring and summer results for the 11 individuals monitored over the two seasons. Table 10 shows that for 1-naphthol and mercury in urine, 4,4'-DDE, PCBs (as Arochlor), and Pb in blood, the spring measurements were significantly predictive of the summer measurements. These results suggest that for these analytes, the environmental sources are stable and/or their elimination kinetics are long-term.

DISCUSSION

The current study provides summary results for the measurement of multiple analytes across 4 pollutant classes in 3 biological media from 18 individuals in 9 homes during the spring of 1993 and a subset of 12 of those same individuals during the summer of 1993. In addition to providing a summary of results, the data are evaluated for seasonal differences, within home and intra-individual variability, and by comparison with NHANES II and III reference data. Interpretation of differences between the current study and the NHANES reference data must be made cautiously, however, since LRGV data differed substantively from NHANES in that two individuals were sampled from each home and sampling was conducted during discrete seasons. For those cases where significant differences were detected or levels were high, the environmental measurements were investigated as a possible explanation. Consistent with the study's scoping objectives, these results and evaluations are intended to support the design of a more focused hypothesis-based study for a larger population.

Seasonal differences

In general, the measurement of nonpersistent pesticide metabolites in urine reflected higher summer time exposures relative to spring. This seasonal difference in environmental levels has been previously observed (Whitmore et al. 1994) and was expected in biomarker measurements due to more frequent use of pesticides during the summer and their relatively fast elimination kinetics. For 2,5-dichlorophenol and 3,5,6-TCP, this seasonal difference was statistically significant ($p \leq 0.10$). For all the analytes, the median summer value always equaled or exceeded the spring value. 2,5-dichlorophenol is a metabolic product of a number of different pesticides including 1,4-dichlorobenzene, dichlofenthion, prothiofos, or phosdiphen. Although the dichlorobenzenes were measured in air, diet, and drinking water, only one indoor air sample was above the method limit of detection in the spring (house 2) and summer (house 4). Similarly, dichlofenthion and prothiofos were measured in dietary samples but none were above the limit of detection. Therefore, a corresponding seasonal difference in environmental media concentrations could not be evaluated.

The chlorpyrifos metabolite, 3,5,6-TCP, was above the limit of detection in 24 of the 29 (83%) person-d sampled over both seasons. This detection rate is similar to the 82% that Hill et al. 1995 observed from NHANES III. Chlorpyrifos was measured in air, house dust, drinking water, and diet, but only in air and house dust was it found at levels above the limit of detection. Consistent with 3,5,6-TCP urine levels, median indoor air chlorpyrifos was higher in the summer (median of 8.3 ng/m^3, n=5) than in the spring (median of 6.9 ng/m^3, n=6). Similarly, for house dust, median summer concentrations (556 ng/g) were higher than spring (299 ng/g) for the six homes measured in both seasons (the air values differ from Mukerjee et al. 1997b because in the current analysis, only homes measured in both seasons were considered, i.e., paired analysis). However, neither the house dust nor the indoor air seasonal differences (Wilcoxon sign rank test) were significant ($p \leq 0.05$).

Table 10. Analytes showing a significant ($p \leq 0.10$) linear regression between biomarker concentrations in spring and in summer.

Analyte[1]	Slope[2]	Intercept[2]	Model
Nonpersistent pesticides (n=11, α/k=0.10/12=0.0083)			
1-Naphthol	0.88 (0.24) p=0.0055	0.150 (0.31) p=0.64	R^2 = 0.594 p=0.0055
Metals in urine (n=11, α/k=0.10/3=0.033)			
Hg	0.98 (0.35) p=0.0189	-1.14 (0.35) p=0.0087	R^2 = 0.44 p=0.0189
Persistent pesticides (n=11, α/k=0.10/10=0.01)			
4,4'-DDE	0.733 (0.21) p=0.0075	0.986 (0.608) p=0.139	R^2 = 0.567 p=0.0075
PCBs as Arochlor 1260	NA	NA	R_{sp} = 0.861 p=0.0007
Metals in blood (n=11, α/k=0.10/1=0.10)			
Pb	0.54 (0.16) p=0.0091	1.19 (0.66) p=0.1068	R^2 = 0.55 p=0.0091

[1] Analytes excluded from analysis due to an insufficient number (i.e., ≤2) of measurements above detection:

Nonpersistent pesticides	Persistent pesticides
2,4,5-Trichlorophenol	2,4'-DDT
2,4,6-Trichlorophenol	4,4'-DDT
2-Isopropoxyphenol	gamma-Hexachlorocyclohexane

[2] Standard error is reported in ( ). Analytes with non-significant correlations ($p \leq 0.10$). When the Shapiro-Wilk statitic indicated a non-normal distribution ($p \leq 0.05$), than the p value from the Spearman correlation is reported (p_{Sp}).

Nonpersistent pesticides and PAH	Metals	Persistent pesticides
7-Carbofuranphenol (p=0.0159)	As (p=0.8745)	trans-Nonachlor (p=0.0378)
2,5-Dichlorophenol (p=0.082)	Cd (p=0.8684)	Heptachlor epoxide (p_{Sp}=0.0183)
2,4-Dichlorophenol (p=0.1069)		Hexachlorobenzene (p_{Sp}=0.0220)
3,5,6-Tichloro-2-pyridinol (p=0.1253)		Oxychlordane (p_{Sp}=0.0190)
2-Naphthol (p=0.8821)		β-Hexachlorocyclohexane (p_{Sp}=0.1341)
2,4-D (p_{Sp} =0.787)		
Pentachlorophenol (p=0.3752)		
4-Nitrophenol (p=0.0750)		
1-Hydroxyprene (p_{Sp}=0.042)		

The indoor air chlorpyrifos concentration was significantly ($p \leq 0.05$) predictive of the urine metabolite levels of the primary and secondary subjects residing within that home. Regression analysis of urine creatinine corrected 3,5,6-TCP on the log of the indoor air concentration was significant (p=0.0001) with an R^2=0.55, a slope of 0.56 (S.E.=0.10) and an intercept of 0.46 (S.E.=0.31) as shown in Fig. 1. The apparent bimodal clustering in indoor air levels is unexplained although it appears not to be seasonally related. The clusters are house and subject specific such that both subjects in homes 3, 4, 9, and 8 are in the higher cluster whereas the subjects within homes 1, 2, 5, 6, and 7 are in the lower cluster. This relationship demonstrates the importance of the indoor environment as a determinant of exposure. No household or activity characteristics (e.g., pets, pesticide use, or air conditioning) could be identified to differentiate the two clusters. Except for homes 6 and 8, all homes reported the use of various pesticides for treatment of cockroaches. Home 4 was the only home to report the use of chlorpyrifos specifically where it was reported to have been used the previous summer.

Similar to indoor air, the concentration of chlorpyrifos in house dust was also predictive of 3,5,6-TCP metabolite levels in urine (Fig. 2). With a correlation coefficient R^2=0.46 (p=0.0001), the Logarithm of the house dust concentration explained slightly less variability than did indoor air. A strong linear correlation (R^2=0.61, p=0.0009) of the log of indoor air on

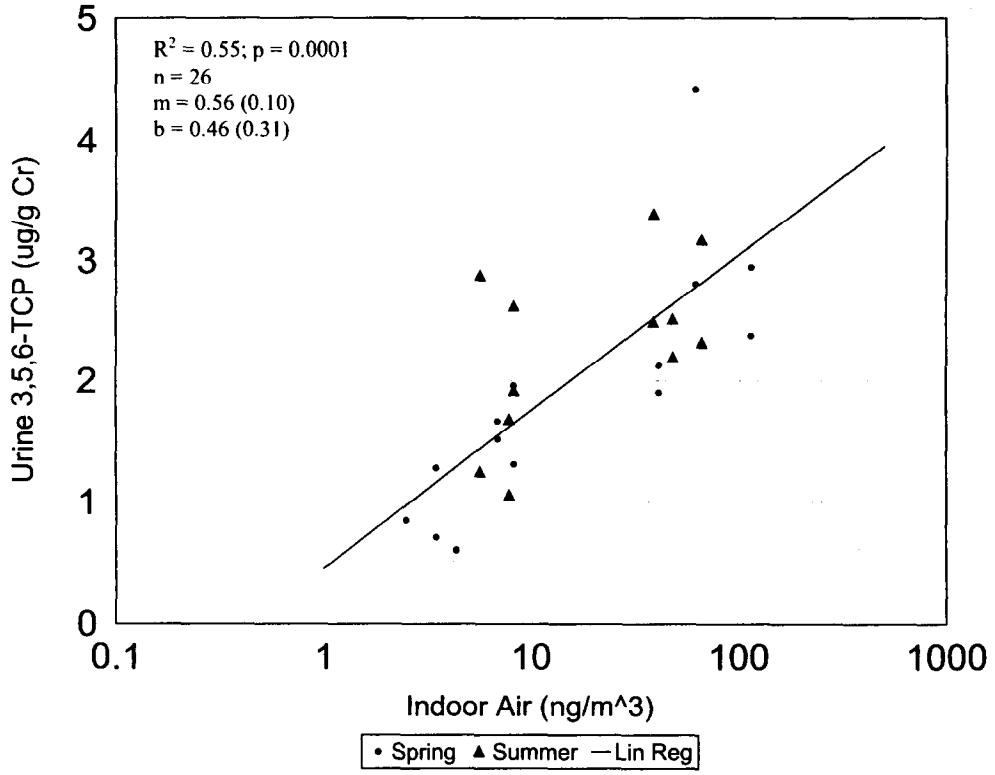

Fig. 1. Regression of urine 3,5,6-TCP on the Log of chlorpyrifos indoor air concentration.

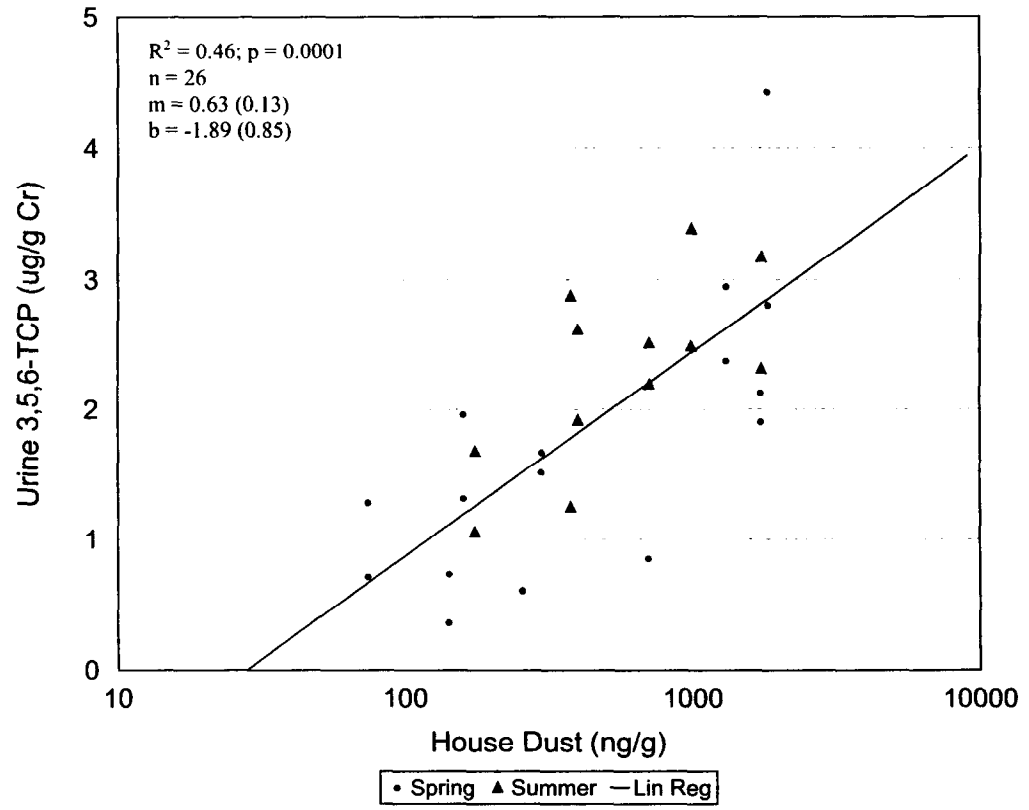

Fig. 2. Regression of urine 3,5,6-TCP on the Log of chlorpyrifos house dust concentration.

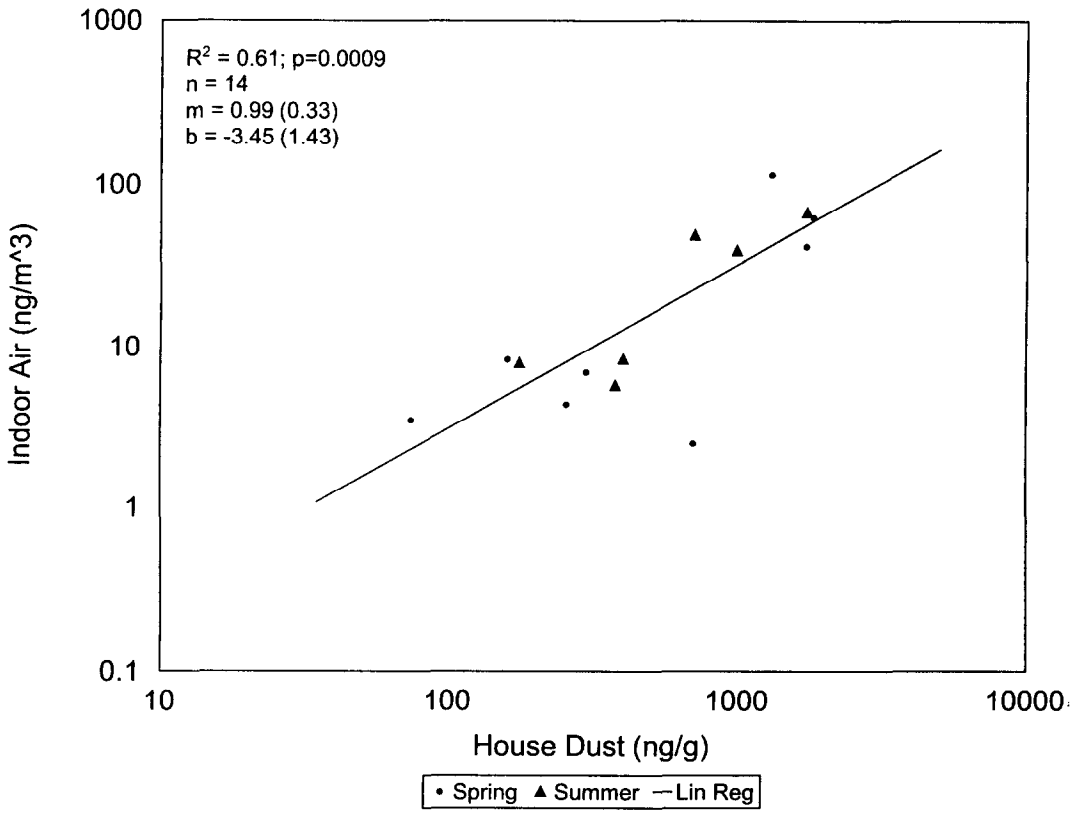

Fig. 3. Regression of indoor air on house dust chlorpyrifos.

the log of the dust concentration suggests that house dust may have been acting as a source for the indoor air contamination which resulted in inhalation exposure and the appearance of 3,5,6-TCP in urine (Fig. 3).

The metals arsenic, cadmium, and mercury and the pyrene metabolite, 1-OHPY, measured in urine were also significantly ($p \leq 0.05$) higher in the summer than in the spring. In environmental media, the metals were either below detection (air, soil, and house dust) and/or measured in only one season (diet, soil, and drinking water) so that it was not possible to evaluate seasonal differences in the environmental media that might correspond to the observed differences in urine.

In contrast, pyrene was detected in most of the air and all of the dust samples, though there was not a statistically significant ($p \leq 0.05$) seasonal difference for either medium (again, Wilcoxon sign rank test). The median concentrations between the two seasons were close among the six homes monitored in both seasons: air 4.0 ng/m^3 and 2.0 ng/m^3; and dust 240 ng/g and 196 ng/g in the spring and summer, respectively (Mukerjee et al. 1997b). Of the remaining relevant environmental media – drinking water, diet, and soil, pyrene could not be evaluated for a seasonal difference because it was below detection, measured only in one season, and unmeasured, respectively. Unlike chlorpyrifos, no significant correlations were observed within or between the urinary metabolite and the environmental media. Although previous studies have demonstrated the importance of diet in PAH environmental exposures and 1-OHPY elimination (Buckley and Lioy 1992; Buckley et al. 1995), since a dietary contribution was undetected in the spring phase and unmeasured during the summer, it is not possible to assess the 1-OHPY variability explained by this pathway.

The trend of generally higher summer biomarker levels as measured in urine was not observed for the persistent pesticides or for lead measured in blood in both seasons. A significant ($p \leq 0.05$) seasonal difference was observed for 1 of 5 pesticides (hexachlorobenzene) where there was sufficient data to evaluate a difference. Similar to what was observed for the non-persistent pesticides, hexachlorobenzene was higher in the summer than in the spring. It was not possible to relate this difference to environmental exposures since this pesticide was not measured in dust or air and it was undetected in drinking water or dietary samples

(Mukerjee et al. 1997b; Berry et al. 1997a, 1997b). Although the seasonal differences in lead levels were not significantly different, the higher median summer blood-Pb relative to spring (3.6 μg/dL versus 3.1 μg/dL) is consistent with previously observed seasonal trends in blood lead levels in children where concentrations were observed to be highest in late June and lowest in March (U.S. EPA 1995). All blood-Pbs were below the 10 μg/dL health threshold guideline established by the CDC.

Intrapersonal seasonal variability

The consistency of an individual's biomarker measurement from spring to summer was evaluated by regressing the paired data. For all the biomarker measurements made in blood and urine over two seasons, a significant regression was observed for 1-naphthol and mercury in urine and 4,4'-DDE, PCBs, and Pb in blood. The stability in biomarker levels from spring to summer observed for these analytes may stem from stability in exposure or from slow elimination kinetics. The water soluble xenobiotics are quickly eliminated in the urine and their persistence is likely attributable to sustained exposure. In contrast, the seasonal correlation for the persistent pesticides and lead is likely enhanced by relatively slow elimination kinetics. This variability is relevant in assessing long-term exposure from single measurements and in defining appropriate exposure sampling strategies.

Comparison to NHANES

NHANES II biomarker measurements were obtained from approximately 4200 persons in 54 locations as a subset of the 28 000 persons surveyed (Murphy and Harvey 1985). As a reference population, the NHANES II and III data provide a valuable basis for gauging the relative exposure among the LRGV study participants. Statistical comparisons based on the percentage of measurements above detection were possible for the nonpersistent pesticides between the current study and NHANES III because of comparability in analytical laboratories and methodologies. Comparisons with NHANES II persistent pesticides are based only on descriptive statistics (i.e., median and maximum values) since the analytical methodology employed in this earlier NHANES study was substantially different from the current study. Even for comparisons with NHANES III where analytical comparability is established, interpretations of observed differences are made cautiously due to differences in sampling strategy (i.e., in LRGV two individuals were sampled in each home and sampling was conducted only during two seasons).

The data suggest that exposures to the two nonpersistent pesticides 4-nitrophenol (summer only) and 2,4-D are elevated in the LRGV sample relative to the reference population represented by NHANES III. Since summer levels of the nonpersistent pesticides tended to be higher, the spring season comparison with NHANES III is conservative. The spring season comparison is also strengthened due to the larger number of persons sampled. 4-nitrophenol is a nonspecific biomarker. The parent compounds giving rise to this metabolite and the environmental media where they were measured included: 4-nitrophenol in drinking water; parathion in air, diet, and house dust; methyl parathion in air, diet, and house dust; nitrobenzene in drinking water; and EPN in diet. Nitrobenzene is an industrial chemical used in the production of aniline and, to a lesser extent, in the production of lubricating oils (ATSDR 1990a). 4-nitrophenol itself has been used as a fungicide, but its principal use is as a chemical intermediate. Of these measurements, only air (summer phase) methyl parathion concentrations had more than 4 values above detection by which to investigate the pathway or source of exposure. Both the Pearson and Spearman correlations of indoor and outdoor air (ng/m^3) on urine levels (ng/L) were nonsignificant ($n=12$, $p \leq 0.10$) suggesting that either the pathway of exposure was not measured or it was not measured with sufficient sensitivity. The highest biomarker levels of 4-nitrophenol were measured in the secondary subjects in home 7 (13.0 μg/g) and 6 (8.8 μg/g). Neither of these subjects were employed in occupations that would explain these exposures (Table 1).

2,4-dichlorophenoxyacetic acid (2,4-D) is a commonly used residential post-emergent acid herbicide. The only environmental medium yielding measurements above detection was house dust and it was only measured in the spring phase. These house dust levels bore no discernable relationship to urine 2,4,-D (e.g., the highest dust concentration of 116 ng/g in HID 9 corresponded to urine levels below detection for both respondents). In the summer, diet and drinking water measurements were made in addition to house dust, although all results were below detection in these media. When a value of half the detection limit was assigned to the balance of 7 and 2 measurements below the limit of detection in urine and dust, respectively (yielding 9 data pairs), neither a significant ($p \leq 0.10$) Spearman nor Pearson correlation was detected. As

was the case in the spring, either the environmental medium serving as the pathway for exposure was not measured or it was not sampled or the analyte was not measured with sufficient sensitivity. In both cases where the biomarker levels appeared high (secondary subjects in homes 4 (1.6 μg/L) and 6 (1.5 μg/L)), occupation did not appear to provide an explanation.

Among the persistent pesticides measured in blood, based on a simple comparison of median and/or 95th percentile values, 4,4'-DDE, trans-nonachlor, and PCBs were higher in the LRGV sample relative to the reference population sampled by NHANES II. 4,4'-DDE is a transformation product (environmental or biological) of DDT and it was one of three biomarkers measured in blood that can be related to DDT exposure. The other two biomarkers, 4,4'-DDT and 2,4'-DDT were not detected with sufficient frequency to be compared to NHANES data. 2,4'-DDT occurs as a contaminant (approximately 15%) in the production of 4,4'-DDT (WHO 1979). All three of these DDT-related contaminants plus the transformation product of 2,4'-DDT, 2,4'-DDE, were measurable in one or more environmental media. In the case of 4,4'-DDE, both the NHANES II median and 95th percentile were exceeded due to high levels measured for both participants in home 5: 145 μg/L measured for the primary participant in the spring and 109 μg/L and 76 μg/L measured for the primary and secondary participant, respectively, in the summer. Specific exposure sources or pathways for 4,4'-DDE could not be identified from the environmental measurements. The observed predictive relationship between blood 4,4'-DDE and 4,4'-DDT suggests that these contaminants are occurring in the environment in a relatively stable proportion and their biotransformation across individuals is similar. The deviation in this relationship for the primary participant in HID 1 may indicate an altered exposure scenario (e.g., exposure to more recent DDT contamination with a higher fraction of DDT to DDE) or an altered metabolism. There was no indication from the questionnaires of any recent exposures for this subject. The elevated levels in the subjects in home 5 might be explained by the primary subject's previous employment as a farm worker although no such exposure was reported in the questionnaires.

The second pesticide that exceeded NHANES 95th percentile was trans-nonachlor found in the secondary subject of home 4 (spring value of 3.49 μg/L) and both subjects in home 5 (primary: 1.74 and 2.03 μg/L; secondary: NA and 1.21 μg/L, spring and summer, respectively). Trans-nonachlor is an environmental or biological transformation product of nonachlor which is an ingredient in technical chlordane. As a termiticide, chlordane was widely used (80% of the market) prior to being banned in April of 1988. Exposure pathways could be evaluated based on measurements of cis- or trans-chlordane (air, diet, drinking water, and house dust) and trans-nonachlor (diet and drinking water). None of the three analytes were measured above detection in any of the water or diet samples. However, in home 4, high levels of cis- and trans-chlordane were found in house dust (average of 1370 ng/g and 1640 ng/g over both seasons, respectively) and indoor air (average of 24 ng/m^3 and 30 ng/m^3 over both seasons, respectively). The indoor air levels for both the cis- and trans-chlordane isomers in this home exceeded median values reported by Mukerjee et al. (1997b) by 25 to 50 fold. Similarly, house dust levels in this home were 50 to 100 times the median. Therefore, in this home there is strong evidence linking high biomarker levels of trans-nonachlor to house dust contamination and volatilization into indoor air. It is of interest to note that within this home, the high blood level of 3.49 μg/L was measured only in the secondary subject (manufacturing worker) during the spring season (0.24 μg/L was measured in the summer). For home 5 where environmental concentrations were near the median and both subjects blood levels were high, diet or previous occupational exposure may have been responsible for the high biomarker measurements.

The current study's elevated PCB levels exceeded NHANES II 95th percentile by about a factor of 3 but were limited to the two participants in HID 7. The 24-h exposure sampling failed to identify possible sources for these high levels. An ancillary diet sample consisting of a locally-caught carp with a dramatic PCB concentration of 399 mg/kg established diet as the likely pathway of exposure. Based on these measurements, state and local government officials conducted additional sampling to verify the source of the contaminated fish and issued an advisory concerning the consumption of fish from that irrigation canal and a nearby reservoir.

In general, the results of blood VOC measurements were within the range of NHANES III reference values. In fact, for some of the more prevalently detected compounds (1,1,-trichloroethane, ethylbenzene, styrene, and tetrachloroethene), the levels measured were actually lower than the reference population. There was some indication that the by-products of chlorination

including dibromochloromethane and, to a lesser extent, bromoform were elevated in LRGV samples. These compounds are not common (found in about 15% of the non-occupationally exposed population) and usually stem from water chlorination used for drinking or swimming (ATSDR 1990b). 2-butanone exceeded the 95th percentile for one subject (the primary subject in HID no 1) with a value of 24 μg/L. This compound is present in paints and surface coatings and it is formed endogenously (ATSDR 1995). Since 2-butanone was not measured in air, it is unclear whether this high value resulted from exposure. CCl_4 was found at detectable levels in the blood of 2 of the 18 individuals measured in the spring (the primary subject in home 2 and the secondary subject in home 6). A source for these two individuals was not apparent since CCl_4 was not detected in drinking water and levels in indoor and outdoor air were not above general ambient background. Neither individual works in an occupation that would be expected to result in exposure.

NHANES comparison data are not yet available for measurements of arsenic or mercury in urine. Kalman et al. (1990) and Clarkson et al. (1988) provide a reference range for biomarker levels of these respective metals. The arsenic assay that was used in the current study did not differentiate between the organic and inorganic species – a differentiation that is critical in evaluating the hazard since the organic form is nonhazardous and frequently present in seafood. Among a set of control homes (n=42) Kalman et al. (1990) sampled multiple occupants four times a year and classified them as self-reported seafood eaters and non seafood eaters. As a conservative comparison to the LRGV results, the group with higher seafood consumption with a median concentration of 10.5 μg/L and a value of 22.4 μg/L at 2 standard deviations above the mean is used as a reference. The LRGV sample exceeded the median value in 7 of 18 cases during the spring and 12 of 12 cases in the summer. Moreover, the mean plus 2 standard deviations was exceeded in 4 of 18 cases in the spring and in all of the cases in the summer. Two extreme values were observed for the secondary (427 μg/L) and primary (82 μg/L) subjects in home 3 during the summer. There was no evidence among the environmental measurements as to possible sources for arsenic since all the air and house dust measurements were below the limit of detection. For these two individuals, additional sampling was conducted and subjects were asked to avoid fish consumption. In this follow-up analysis, arsenic levels dropped to near the LRGV median value of 27.2 μg/L providing strong evidence that the exposure was dietary and nontoxic. Arsenic in the diet was measured only in the spring and only a single sample (primary respondent in HID 7) was measured above detection with a value of 43.6 μg/d (Berry et al. 1997). This sample corresponded to the participant's self-reported inclusion of a "tuna patty" in the 24-h diet. Drinking water, also only measured in the spring, yielded detectable results in six of nine homes (Berry et al. 1997b), however, the range of values above detection was narrow, 1.1-4.5 μg/L, and no correlation with the urine values was observed. The absence of detectable levels in house dust or air implicate diet as the likely source of the nonhazardous organoarsenic compounds.

Clarkson et al. (1988) reports a median mercury concentration of <0.5 μg/L, a 95th percentile value of 20.0 μg/L, and a maximum value of 221 μg/L from a worldwide survey of persons with no known exposure. The current study results ranged from 0.2 to 6.9 μg/L in the spring and 2.5 to 8.6 during the summer – all values well below the 95th percentile for this comparison study.

The significant correlation (R^2=0.31; n=18, p=0.016) between blood and urine mercury was expected since both media provide good measures of absorbed inorganic mercury (Langworth et al. 1991). The large fraction of unexplained variability is likely due to differences in elimination kinetics and partitioning between the two media for mercury of various forms. For example, blood mercury, comprising bound inorganic and methyl mercury, is a better indicator of dietary mercury (usually in the form of methyl mercury) whereas almost no methyl mercury is excreted in urine due to its low water solubility.

Like mercury, cadmium was also measured in blood and urine. Whereas comparison data was available from NHANES III for urine levels, blood concentrations are compared to a reference population used in a study investigating the impact of a smelter on a community (Wyowski et al. 1978). This investigation reported a median blood concentration of 0.5 μg/L (range: 0.4-2.7 μg/L) among nonsmoking adults (>40 y). The LRGV samples are well below this reference range with a median concentration of <0.2 μg/L (the LOQ) and a max_2 value of 0.5 μg/L.

Elevated biomarker levels across pollutant classes appear uniform across study subjects. The secondary subject in home 6 appears to be at greatest risk from

high-level exposure to multiple pollutants (4-nitrophenol, 2,4-D, and CCl_4). Occupation does not appear to provide an explanation for these exposures.

Some pesticides that could not be measured in biological samples were commonly found in environmental samples. The pesticides detected ≥50% in one or more environmental media but without a method of detection in blood or urine included: permethrin (cis and trans), atrazine, diazinon, dieldrin, and malathion. The absence of biological monitoring methods for these environmentally prevalent pesticides provides a line of justification for their development.

CONCLUSIONS

The LRGV study was designed as a feasibility or range finding investigation to generally characterize residential environmental contamination and associated biomarker levels in order to aid in the design of future studies in the region. The number of subjects was small and nonrepresentative but the environmental and biomarker characterization was extensive involving the measurement of metals, pesticides, VOCs, PAHs, and PCBs in multiple environmental and biological media.

Differences in biomarker levels were observed between spring and summer for the 12 individuals sampled in both seasons. For the metals cadmium, mercury, and arsenic, the pyrene metabolite, 1-OHPY, and nonpersistent pesticides in urine, exposures were generally higher in summer than in spring. This conclusion is based on a combination of descriptive comparisons (median and maximum values) and nonparametric statistics (Wilcoxon sign rank test). Because of the small sample size, it is likely that only large differences would be detected by the sign rank test. This same seasonal pattern was not detected for the persistent pesticides or lead measured in blood serum.

Some differences exist between the sampling strategy of the current study and the NHANES III reference which may confound true differences between the two studies. However, their comparison is consistent with the scoping nature of the LRGV study to investigate biomarker levels relative to a large reference population. In this context, LRGV biomarker levels of 4-nitrophenol, 2,4-D, and CCl_4 were detected with greater frequency ($p \leq 0.10$) than would have been expected from the NHANES III reference data. A comparison of LRGV descriptive statistics (median and 95th percentile) with reference values identifies arsenic, 4,4'-DDE, trans-nonachlor, and PCBs as possible contaminants to be considered for further investigation. These findings may provide the basis for formulating specific hypotheses to be tested in future population-based studies planned for the region.

In general, it was not possible to link seasonal differences or elevated biomarker levels to environmental concentrations due to a low frequency of detection and/or absence of the measurement altogether. Chlorpyrifos measured in air and house dust, and its metabolite, 3,5,6-TCP measured in urine was an exception where biomarker levels were found to be strongly linked to indoor air and house dust contamination.

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Disclaimer—This paper has been reviewed in accordance with the U.S. Environmental Protection Agency's peer and administrative review policies and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

REFERENCES

Akland, G.G.; Schwab, M.; Zenick, H.; Pahl, D.A. An interagency partnership applied to the study of environmental health in the Lower Rio Grande Valley of Texas. Environ. Int. 23: 595-609; 1997.

Ashley, D.L.; Bonin, M.A.; Cardinali, F.L.; McCraw, J.M.; Holler, J.S.; Needham, L.L.; Patterson, D.G. Determining volatile organic compounds in human blood from a large sample population using purge and trap chromatography/mass spectrometry. Anal. Chem. 64: 1021-1029; 1992.

Ashley, D.L.; Bonin, M.A.; Cardinali, F.L.; McCraw, J.M.; Wooten, J.V. Blood concentrations of volatile organic compounds in a nonoccupationally exposed US populations and in groups with suspected exposure. Clin. Chem. 40(7): 1401-4; 1994.

ATSDR (Agency for Toxic Substances and Disease Registry). Public health statement for nitrobenzene. Atlanta, GA: U.S. Dept. of Health and Human Services, Public Health Service, ATSDR; 1990a.

ATSDR (Agency for Toxic Substances and Disease Registry). Public health statement for bromoform and chlorodibromomethane. Atlanta, GA: U.S. Dept. of Health and Human Services, Public Health Service, ATSDR; 1990b.

ATSDR (Agency for Toxic Substances and Disease Registry). ToxFAQs for 2-butanone. Atlanta, GA: U.S. Dept. of Health and Human Services, Public Health Service, ATSDR; 1995.

Berry, M.R.; Johnson, L.S.; Brenner, K.P.; Thomas, K.W. Dietary characterizations in a study of human exposures in the Lower Rio Grande Valley: II. Household waters. Environ. Int. 23: 693-703; 1997a.

Berry, M.R.; Johnson, L.S.; Jones, J.W.; Rader, J.I.; Kendall, D.C.; Sheldon, L.S. Dietary characterizations in a study of human exposures in the Lower Rio Grande Valley: I. Foods and beverages. Environ. Int. 23: 675-692; 1997b.

Buckley, T.J.; Lioy, P.J. An examination of the time course from human dietary PAH exposure to urinary elimination of 1-hydroxypyrene. Br. J. Ind. Med. 49: 113-124; 1992.

Buckley, T.J.; Waldman, J.M.; Dhara, R.; Greenberg, A.; Ouyang, Z.; Lioy, P.J. An assessment of a urinary biomarker for total human environmental exposure to benzo[a]pyrene (BaP). Int. Arch. Occup. Environ. Health 67: 257-266; 1995.

Burse, V.W.; Groce, D.F.; Korver, M.P.; McClure, P.C.; Head, S.L.X.; Needham, L.L.; Lapeza, C.R.; Smrek, A.L. Use of reference pools to compare the qualitative and quantitative determination of polychlorinated biphenyls by packed and capillary gas chromatography with electron capture detection. Part 1. Serum. Analyst 115: 243-251; 1990a.

Burse, V.W.; Head, S.L.; Korver, M.P.; McClure, P.C.; Donahue, J.F.X.; Needham, L.L. Determination of selected organochlorine pesticides and polychlorinated biphenyls in human serum. J. Anal. Toxicol. 14: 137-142; 1990b.

Burse, V.W.; McClure, P.C.; Korver, M.P.; Head, S.L.; Needham, L.L. Potential compounds for monitoring method performance in the determination of selected organochlorine pesticides and polychlorinated biphenyls in human serum. J. Anal. Toxicol. 14: 143-145; 1990c.

Camann, D.E.; Harding, H.J.; Lewis, R.G. Trapping of particle-associated pesticides in indoor air by polyurethane foam and exploration of soil track-in as a pesticide source. In: Proc. fifth international conference on indoor air quality and climate. Toronto. 1990: 621-626. Available from: Canada Mortgage and Housing Association, Toronto, Canada.

Clarkson, T.; Hursh, J.B.; Sager, P.R.; Syversen, T.L.M. Mercury. In: Clarkson, T.W.; Friberg, L.; Nordber, G.F.; Sager, P.R., eds. Biological monitoring of toxic metals. New York: Plenum Press; 1988: 166-246.

Fenske, R.A.; Elkner, K.P. Multi-route exposure assessment and biological monitoring of urban pesticide applicators during structural control treatments with chlorpyrifos. Toxicol. Ind. Health 6: 349-371; 1990.

Fenske, R.A.; Black, K.G.; Elkner, K.P.; Lee, C.L. Potential exposure and health risks of infants following indoor residential pesticide applications. Am. J. Public Health 80: 689-693; 1990.

Göen, Th.; Gündel, J.; Schaller, K.H.; Angerer, J. The elimination of 1-hydroxypyrene in the urine of the general population and workers with different occupational exposures to PAH. Sci. Total Environ. 163: 195-201; 1995.

Greenwood, M.R.; Clarkson, T.W.; Farant, J.P.; Chartrand, A.; Khayat, A. Epidemiological experience with the Magos' reagent in the determination of different forms of mercury in biological samples by flameless atomic absorption. J Anal. Toxicol. 1: 265-269; 1977.

Hill, R.H.; To, T.; Holler, J.S.; Fast, D.M.; Smith, S.J.; Needham, L.L.; Binder, S. Residues of chlorinated phenols and phenoxy acid herbicides in the urine of Arkansas children. Arch. Environ. Contam. Toxicol. 18: 469-474; 1989.

Hill, R.H.; Head, S.L.; Baker, S.; Gregg, M.; Shealy, D.B.; Bailey, S.L.; Williams, C.C.; Sampson, E.J.; Needham, L.L. Pesticide residues in urine of adults living in the United States: Reference range concentrations. Environ. Res. 71: 99-108; 1995.

Holler, J.S.; Fast, D.M.; Hill, R.H.; Cardinali, F.L.; Todd, G.D.; McCraw, J.M.; Bailey, S.L.; Needham, L.L. Quantification of selected herbicides and chlorinated phenols in urine by using gas chromatography/mass spectrometry/mass spectrometry. J. Anal. Toxicol. 13: 152-157; 1989.

Jayanty, R.K.M.; Albritton, J.R.; Straley, Y.H.; von Lehmden, D.J. Stability of PPB and P.M. organic cylinder gases used for calibration and audits. J. Air Waste Manage. Assoc. 42: 1198-1203; 1992.

Kalman, D.; Huges, J.; van Belle, G.; Burbacher, T.; Bolgiano, D.; Coble, K.; Mottet, N.K.; Polissar, L. The effect of variable environmental arsenic contamination on urinary concentrations of arsenic species. Environ. Health Persp. 89: 145-151; 1990.

Langworth, S.; Elinder, C.G.; Gothe, C.J.; Vesterberg, O. Biological monitoring of environmental and occupational exposure to mercury. Int. Arch. Occup. Environ. Health 63:161-167; 1991.

Lebowitz, M.D.; O'Rourke, M.K.; Gordon, S.; Moschandreas, D.; Buckley, T.J.; Nishioka, M. National Human Exposure Assessment Survey (NHEXAS): Population-based exposure measurements in Arizona. J. Exposure Anal. Environ. Epidemiol. 5: 297-325; 1995.

Levin, J.O.; Rhén, M.; Sikström, E. Occupational PAH exposure: Urinary 1-hydroxypyrene levels of coke oven workers, aluminum smelter pot-room workers, road pavers, and occupationally non-exposed persons in Sweden. Sci. Total Environ. 163: 169-177; 1995.

Lewis, R.G.; Fortmann, R.C.; Camann, D.E. Evaluation of methods for monitoring the potential exposure of small children to pesticides in the residential environment. Arch. Environ. Contam. Toxicol. 26: 37-46; 1994.

Lindstrom, A.B.; Pleil, J.D. Alveolar breath sampling and analysis to assess exposures to methyl tertiary butyl ether (MTBE). J. Air Waste Manage. Assoc. 46: 676-682; 1996.

Lioy, P.J.; Assessing total human exposure to contaminants. Environ. Sci. Technol. 24: 938-945; 1990.

Lippmann, M.; Thurston, G.D. Exposure assessment: Input into risk assessment. Arch. Environ. Health 43(2): 113-123; 1988.

Littlejohn, D.; Fell, G.S.; Ottaway, J.M. Modified determination of total and inorganic mercury in urine by cold vapor atomic absorption sectrometry. Clin. Chem. 22: 1719-1723; 1976.

Miller, D.T.; Paschal, D.C.; Gunter, E.W.; Stroud, P.E.; D'Angelo J. Determination of lead in blood using electrothermal atomization atomic absorption spectrometry with a L'vov platform and matrix modifier. Analyst 112: 1701-1704; 1987.

Mukerjee, S.; Ellenson, W.D.; Lewis, R.G.; Stevens, R.K.; Somerville, M.C.; Shadwick, D.S. An environmental scoping study in the Lower Rio Grande Valley of Texas. I. Comparative assessment of air sampling methods. Environ. Int. 23: 611-628; 1997a.

Mukerjee, S.; Ellenson, W.D.; Lewis, R.G.; Stevens, R.K.; Somerville, M.C.; Shadwick, D.S.; Willis, R.D. An environmental scoping study in the Lower Rio Grande Valley of Texas. III. Residential microenvironmental monitoring for air, house dust, and soil. Environ. Int. 23: 657-673; 1997b.

Murphy, R.; Harvey, C. Residues and metabolites of selected persistent halogenated hydrocarbons in blood specimens from a general population survey. Environ. Health Persp. 60: 115-120; 1985.

Murphy, R.S.; Kutz, F.W.; Strassman, S.C. Selected pesticide residues or metabolites in blood and urine specimens from a general population survey. Environ. Health Persp. 48: 81-86; 1983.

NRC (National Research Council). Risk assessment in the federal government: Managing the process. Washington, D.C.: National Academy Press; 1983.

NRC (National Research Council). Frontiers in assessing human exposures to environmental toxicants. Washington, D.C.: National Academy Press; 1991a.

NRC (National Research Council). Monitoring human tissues for toxic substances. Washington, D.C.: National Academy Press; 1991b.

NRC (National Research Council). Human exposure assessment for airborne pollutants, advances and opportunities. Washington, D.C.: National Academy Press; 1991c.

Ott, W.R. Total human exposure: Basic concepts, EPA field studies, and future research needs. J. Air Waste Manage. Assoc. 40: 966-975; 1990.

Paschal, D.C.; Bailey, G.G. Determination of urinary arsenic by electrothermal atomic absorption with the L'vov platform and matrix modification. Analytica Chimica Acta. 181: 179-186; 1986.

Pellizzari, E.; Lioy, P.; Quackenboss, J.; Whitmore, R.; Clayton, A.; Freeman, N.; Waldman, J.; Thomas, K.; Rodes, C.; Wilcosky, T. Population-based exposure measurements in EPA Region 5: A phase I field study in support of the National Human Exposure Assessment Survey. J Exp. Anal. Environ. Epidemiol. 5: 297-325; 1995.

Pirkle, J.L.; Sampson, E.J.; Needham, L.L.; Patterson, D.G.; Ashley, D.L. Using biological monitoring to assess human exposure to priority toxicants. Environ. Health Persp. 103: 45-48; 1995.

Presidential/Congressional Commission on Risk Assessment and Risk Management. Framework for environmental health risk management. Final Report. Vol. 1. Washington, D.C.; 1997.

Pruszkowska, E.; Carnrick, G.R.; Slavin, W. Direct determination of cadmium in urine with use of a stabilized temperature platform furnace and Zeeman background correction. Clin. Chem. 29: 477-480; 1983.

Racke, K.D. Environmental fate of chlorpyrifos. Rev. Environ. Contam. Toxicol. 131: 1-150; 1993.

Raymer, J.H.; Thomas, K.W.; Cooper, S.D.; Whitaker, D.A.; Pellizzari, E.D. A device for sampling of human alveolar breath for the measurement of expired volatile organic compounds. J. Anal. Toxicol. 14: 337-344; 1990.

Roinestad, K.S.; Louis, J.B.; Rosen, J.D. Determination of pesticides in indoor air and dust. J. AOAC Int. 76(5): 1121-6; 1993.

Rosner, B. Multisample inference. Chapter 9. In: Fundamentals of biostatistics. 4th Edition. New York: Buxbury Press; 1995.

Schaller, K.H.; Angerer, J.; Hausmann, N. The determination of 1-hydroxypyrene in urine as a tool for the biological monitoring of PAH-exposed persons. In: Garrigues, P.; Lamotte, M., eds. Polycyclic aromatic compounds, synthesis, properties, analytical measurements, occurrence and biological effects. Langhourne, PA: Gordon and Breach Science Publishers; 1993: 1023-1030.

Sexton, K.; Callahan, M.A.; Bryan, E.F. Estimating exposure and dose to characterize health risks: The role of human tissue monitoring in exposure assessment. Environ. Health Persp. 103(3): 13-29; 1995.

Stehr-Green, P.A. Demographic and seasonal influences on human serum pesticide residue levels. J. Toxicol. Environ. Health 27: 405-421; 1989.

Stoeppler, M.; Brandt, K. Contributions to automated trace analysis. Part V. Determination of cadmium in whole blood and urine by electrothermal atomic absorption spectrophotometry. Fresenius Z. Anal. Chem. 300: 372-380; 1980.

Thomas, K.W.; Pellizzari, E.D.; Cooper, S.D. A canister-based method for collection and GC/MS analysis of volatile organic compounds in human breath. J. Anal. Toxicol. 15: 54-59; 1991.

U.S. EPA (U.S. Environmental Protection Agency). Future risk: Research strategies for the 1990's. SAB-EC-88-040. Washington, D.C.: Science Advisory Board; 1988.

U.S. EPA (U.S. Environmental Protection Agency). Lower Rio Grande Valley environmental monitoring study: Report to the community on the pilot project. RTP, NC: National Exposure Research Laboratory; 1994.

U.S. EPA (U.S. Environmental Protection Agency). Seasonal rhythms of blood-lead levels: Boston, 1979-1983. EPA747-R-94-003. Washington, D.C.; 1995.

Viau, C.; Vyskočil, A.; Martel, L. Background urinary 1-hydroxypyrene levels in non-occupationally exposed individuals in the Province of Quebec, Canada, and comparison with its excretion in workers exposed to PAH mixtures. Sci.Total Environ. 163: 191-194; 1995.

Wallace, L.A.; Pellizzari, E.D.; Harwell, T.D.; Whitmore, R.; Sparacino, C.; Zelon, H. Total exposure assessment methodology (TEAM) study: Personal exposures, indoor-outdoor relationships, and breath levels of volatile organic compounds in New Jersey. Environ. Int. 12: 369-387; 1986.

Whitmore, R.W.; Immerman, F.W.; Camann, D.E.; Bond, A.E.; Lewis, R.G.; Schaum, J.L. Non-occupational exposures to pesticides for residents of two cities. Arch. Environ. Contam. Toxicol. 26: 47-59; 1994.

WHO (World Health Organization). Environmental health criteria 9: DDT and its derivatives. Geneva: World Health Organization; 1979.

Wysowski, D.K.; Landrigan, P.J.; Ferguson, S.W.; Fontaine, R.E.; Tsongas, T.A.; Porter, B. Cadmium exposure in a community near a smelter. Am. J. Epidemiol. 107: 27-35; 1978.

Zhao, Z.; Quan, W.; Tian, D. The relationship between polynuclear aromatic hydrocarbons in ambient air and 1-hydroxypyrene in human urine. J. Environ. Sci. Health A27(7): 1949-1966; 1992.