Assessing Exposure to Air Toxics Relative to Asthma

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Asthma is a respiratory disease whose prevalence has been increasing since the mid 1970s and that affects more than 14.6 million residents of the United States. Environmental triggers of asthma include air pollutants that are respiratory irritants. Air toxics emitted into the ambient air are listed in the 1990 Clean Air Act Amendments as hazardous air pollutants (HAPs) if they can adversely affect human health, including the respiratory tract. HAPs include particulate and gaseous-phase pollutants, individual organic compounds and metals, and mixtures. Associations between asthma exacerbation and both particles and indoor volatile organic compounds (VOCs), often referred to as indoor air quality, have been reported. Studies conducted in the United States, Canada, and Europe over the past two decades have shown that most people living in the developed countries spend the majority of their time indoors and that the air concentrations of many air toxics or HAPs are higher indoors than in the ambient air in urban, suburban, and rural settings. Elevated indoor air concentrations result from emissions of air toxics from consumer products, household furnishings, and personal activities. The Relationship of Indoor, Outdoor and Personal Air (RIOPA) study was designed to oversample homes in close proximity to ambient sources, excluding residences where smokers lived, to determine the contribution of ambient emissions to air toxics exposure. The ratios of indoor to outdoor air concentrations of some VOCs in homes measured during RIOPA were much greater than one, and for most other VOCs that had indoor-to-outdoor ratios close to unity in the majority of homes, elevated ratios were found in the paired samples with the highest concentration. Thus, although ambient emissions contribute to exposure of some air toxics indoors as well as outdoors, this was not true for all of the air toxics and especially for the higher end of exposures to most volatile organic air toxics examined. It is therefore critical, when evaluating potential effects of air toxics on asthma or other adverse health end points, to determine where the exposure occurs and the source contributions for each air toxic and target population separately and not to rely solely on ambient air concentration measurements. *Key words:* **ambient emissions, exposure, indoor air, particles, RIOPA study, VOC, volatile organic compounds.** *Environ Health Perspect* **110(suppl 4):527–537 (2002).**
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Asthma is a common respiratory disease that affects children and adults but is without a universal definition because of a poor understanding of its causes, natural history, and pathology (*1*). It is characterized by chronic inflammation with infiltration of lymphocytes, eosinophils, and mast cells and thickening and disorganization of tissues of the airway walls, broncoconstriction, mucus secretion, and increased airway responsiveness to stimuli. These respiratory responses result in the narrowing of the airways, causing difficult in breathing (*1*). Asthma is a chronic disease whose prevalence has been increasing since the mid 1970s, affecting more than 14.6 million individuals within the United States (*2*). The cause of the increased prevalence has not been definitively established. Environmental agents, along with genetic considerations, have been suggested as both causing asthma and exacerbating existing conditions. Environmental agents include antigens from dust mites, cockroaches, and mold, weather condition changes, and air pollutants such as the criteria pollutants ozone, sulfur dioxide, particulate matter (PM), and nitrogen dioxide and hazardous air pollutants (HAPs) (*3*). Although the evidence for a causal association between air pollutants and asthma is weak, evidence for exacerbation of asthma by air pollutants, particularly the criteria pollutants, has been reported for controlled clinical trials and epidemiologic studies (*3–9*). Few studies have examined the role of ambient HAPs on asthma exacerbation. Individual HAPs are present in the ambient environment at significantly lower concentrations than the criteria pollutants and are often present at higher concentrations in indoor air than in outdoor air. The presence of criteria pollutants along with HAPs in the ambient air of cities makes it difficult to distinguish the effects of HAPs from those of the criteria pollutants or to determine if there is an interactive effect.

The ambient concentrations of many air pollutants have declined in urban areas of developed countries, whereas the incidence of reported asthma has increased. This suggests that these air pollutants are not the cause, or only cause, of asthma, although this does not preclude their role in asthma exacerbation. Many of the compounds listed as HAPs are included because of cancer end points due to chronic exposures, but others have noncancer end points for acute and chronic exposure, including effects on the respiratory system (*10,11*). Compounds with noncancer, acute end points include oxygenated volatile organic compounds (VOCs; e.g., aldehydes, ethers, and oxides), reactive VOCs (e.g., acrolein, hydrazine, and phosgene), and organic and inorganic acids (*10*). Additional HAPs have reported respiratory effects for chronic exposures and at high concentrations are respiratory irritants. HAPs can produce nonspecific respiratory responses. Thus, the combined concentrations may need to be considered when evaluating asthma exacerbation and not just exposure to individual compounds. It has been known for more than a decade that exposures to the mixture of VOCs present in indoor air, which include many HAPs such as aromatic and chlorinated organic compounds, can irritate the mucus membrane in the respiratory tract in both healthy and sensitive individuals (*12*). Whether individual HAPs penetrate into the lungs and can potentially affect asthmatic individuals, or only affect the upper portion of the respiratory tract because of solubility considerations, needs to be considered in extrapolating respiratory irritation to asthma exacerbation. Further, differences in exposures by location and cumulative exposure of multiple HAPs that may have the same mechanism of action should be considered in the evaluation of potential adverse effects of HAPs on asthmatic individuals.

Physical activity level is also an important consideration in determining the dose of an air pollutant. Physical exertion increases breathing rates and causes pollutants to penetrate deeper into the lungs. Physical activity has been shown to cause greater symptoms in

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asthmatic individuals exposed to ozone than when they are at rest (*13*). Physical activity occurs outdoors more frequently than indoors. Therefore, a final evaluation of the association between asthma exacerbation and air pollutants should consider not only differences in concentration with location but also the activity level in each location. This does not address the issue of how physical activity varies with location, microenvironment, and time of year and its role in exposure and asthma. Rather, it is a review of the magnitude of HAP exposures in different locations to help provide guidance in understanding the potential role of ambient air concentrations of HAPs on asthmatic individuals and to establish sources of HAP exposures.

Concepts of Exposure

Human exposure to air toxics occurs when individuals breathe air containing these constituents. The concentrations of air toxics vary with time and location, and as people move among locations and activities, the resultant exposure changes. Further, the contributions by different sources to exposure to air toxics vary with location. The amount of pollutant delivered to the lung depends on the person's breathing rate. Thus, activity level can be an important consideration in determining the potential exposure and dose delivered to the lung, the site of concern for asthmatic individuals. Inhalation exposure has been defined as the integral of the concentrations as a function of time over the time period of interest for each individual (*14*):

$$E = \int_{t_1}^{t_2} c(t)dt, \qquad [1]$$

where E is exposure, $c(t)$ is the concentration being encountered as a function of time, and t_1 and t_2 are the starting and ending time of the exposure, respectively.

When determining exposure, it is therefore important for investigators to measure the air concentrations of air toxics reaching individuals or a population and not just the concentration in the ambient atmosphere, if it is possible that the two may differ. Two approaches, direct and indirect, have been taken to measure inhalation exposure (*15*). With the direct measurement method a personal monitor is worn in the breathing zone to either continually collect for subsequent analysis or directly measure the concentration of the pollutant for the defined exposure period. The indirect method uses measurements of the air concentrations in all the locations or "microenvironments" encountered by an individual or population and determines, typically with diaries, the amount of time spent in each microenvironment. The concept of microenvironments is also critical in developing procedures for exposure modeling and recognizes that people are mobile and that concentrations of air toxics are not the same in all locations. Microenvironments have typically been defined as individual or aggregate locations or even as activities taking place within a location, where a homogeneous concentration of the target pollutant exists. This concept of a microenvironment is one of a perfectly mixed or idealized compartment of classical compartmental modeling. Because microenvironments can have gradients in air toxic concentrations, particularly when sources exist in the microenvironment, more recent and general definitions view the microenvironment as a volume of air that can be fully characterized by a set of either mechanistic or phenomenologic governing equations, when properly parameterized, given appropriate initial and boundary conditions (*16*).

Microenvironments used to determine air toxics exposures typically include indoor residences, indoor work environment, other indoor locations, outdoors near residences, other outdoor locations, and in vehicles. The in-vehicle microenvironment is often segregated from other locations because of air toxic emissions from mobile sources. Indoor residences, indoor work environment, and outdoors near residences are typically separated from other indoor and outdoor locations because of the time spent there and potential differences between the residential, work, and public environments. The exposure in a microenvironment is calculated using a formula analogous to Equation 1 but as the sum of the discrete product of "representative" concentrations for the individual or activity being examined in that microenvironment times the duration of time spent there:

$$E = \sum_{i=1}^{n} c_i \Delta t_i, \qquad [2]$$

where i are microenvironments from 1 to n, c_i is the concentration in the ith microenvironment, and Δt_i is the duration spent in the ith microenvironment. The daily exposure is the sum of the exposures in all microenvironments encountered within a day. The exposure calculated is representative of the true exposure provided that all microenvironments that contribute significantly to the total exposure are included and the concentration assigned to the microenvironment is appropriate for the time period spent there. In addition to measurement of exposure, exposure modeling is employed for both individuals and populations. Exposure modeling is used to determine exposures to large populations because it often is not financially practical to make a sufficient number of exposure measurements to completely characterize the spatial and temporal range of exposures in large populations, and to predict what changes in emissions or activities are most effective to obtain reduced exposure. A discussion of the underlying principles of exposure modeling is beyond the scope of this article. However, it is important for investigators, when examining an association between exposure to air toxics and an adverse health effect, to determine how best to reduce emissions of HAPs to establish where exposures occur and their sources. Thus, as discussed in this article, a complete evaluation of exposure is necessary, and not solely a measure of ambient air concentrations and emissions.

Ambient Air Toxics and Asthma

The 1990 Clean Air Act Amendments (*17*) list 188 HAPs or air toxics. These include heavy metals (predominantly particulate components, except for mercury, which has a gaseous phase), organic compounds (which include both volatile and particulate components), and pesticides (*18*). HAPs are emitted into the ambient air from thousands of sources, including large and small stationary sources, area sources, and mobile sources. The HAPs emitted to the ambient air result in potential inhalation exposure in urban settings where they are emitted or when transported through regional, national, or global air sheds, depending on their atmospheric residence time. Although much of the focus of health concerns on HAPs has been toward cancer end points, some of the agents can be respiratory irritants that may exacerbate or potentially cause asthma. On a broad scale, in 1993 3.7 million tons of HAPs were emitted, with approximately 41% from mobile sources, 35% from area sources, and 24% from point sources (*18*). A comparison of emissions by state shows that, as expected, industrial and highly populated areas have the highest emissions. The largest sources of HAPs are mobile sources—on-road vehicles—that emit acetaldehyde, benzene, 1,3-butadiene, formaldehyde, toluene, xylenes, and particles.

Chemicals are classified as air toxics because of suspected associations with adverse health outcomes, including respiratory problems. Nearly 50 million people are estimated to live in locations where the estimated ambient concentrations of one or more HAPs exceed levels of concern for noncancer health effects in humans (*19*). Environmental agents that may provoke bronchospasm attacks include irritant gases, inorganic particles, allergens, and infections (*20*). It is less clear whether the same

environmental factors also cause asthma. There are both seasonal patterns and day-to-day variations in asthma exacerbation. Although the seasonal variability is likely related to respiratory virus infection, the day-to-day variations may be more closely associated with environmental factors, including air pollution. Higher prevalence of asthma and allergic disease and greater number of admissions to hospitals and clinics for asthma attacks have been reported among children living close to busy roads or heavy truck traffic (*21–23*). Such an association would suggest that ambient emissions of air toxics or particulate matter (PM) may aggravate asthma. Other studies, however, have not found an association between asthma diagnosis, treatment, or hospital admissions and living close to traffic (*24,25*).

Indoor Air Toxics and Asthma

It has been proposed that asthmatic symptoms may be caused by indoor VOCs and formaldehyde (*26–28*). A European Community respiratory health survey was used to identify individuals with (n = 47) and without (n = 41) asthma for whom an exposure assessment was done (*26*). Both apartments and single-family homes with a variety of heating sources were included. Indoor tobacco smoking was reported in 21% of the homes. Presence of dust mites and visible signs of dampness or microbial growth were significantly related to asthma symptoms. Nocturnal breathlessness was found to be associated with the presence of wall-to-wall carpeting and formaldehyde concentration, which was presumably from indoor sources. Increases in a variety of symptoms related to asthma were significantly associated with concentrations of total VOCs, formaldehyde, and various subclasses of VOCs (substituted aromatic compounds), *n*-alkanes, terpenes, butanols, and low–boiling-point hydrocarbons). However, correlations were also identified between the VOCs and the presence of dust mites, which could have confounded the results. One suggested explanation for the stronger association between indoor air quality and nocturnal breathing symptoms compared with daytime asthma symptoms was the greater amount of time spent at home during the night than during the day. Other explanations included higher nighttime indoor air concentrations and greater susceptibility to symptoms at night. VOCs emitted from newly painted surfaces have been reported to be associated with asthmatic symptoms in painters (*27*) and residents (*28*). Associations of VOC exposures at air concentrations of 25 mg/m^3 with both inflammation and obstructive reaction in airways have been found in controlled chamber studies (*29,30*). The controlled chamber air concentration was higher than that measured in homes where relationships between asthma and VOCs have been reported, but the exposure time was shorter. Formaldehyde has been observed to cause abnormal variability in peak expiratory flow (*31*), but there have been inconsistent reports on its role in exacerbating or causing asthma (*32–34*). Environmental tobacco smoke has also been identified as an indoor environmental trigger for many asthma patients, although there is only limited documentation of the effects of passive smoke on asthma (*35,36*). Environmental tobacco smoke contains a large number of air toxics (*37*). It is suggested that the role of passive smoking as an initiator is related more closely to transient "wheezy bronchitis" than to "allergic asthma." Its association with symptom prevalence and asthma severity in school age children probably reflects a role as a trigger of symptomatic episodes. Passive smoking increases exposure to both particles and volatile organic air toxics and is a major source of indoor air pollution. Proximity to industrial emissions of VOCs has been linked to increased asthma (*38*). These studies suggest that various HAPs (e.g., aromatic hydrocarbons, formaldehyde, diesel particles) or combinations can exacerbate asthma.

Duration of Exposure and Asthma Exacerbation

It is unclear whether short peak exposures to lung irritants of minutes or longer exposures of hours to days, or both, may be responsible for reported associations between asthma symptoms and air pollution. Because of the low air concentrations of air toxics, sampling duration is typically 12–48 hr. Thus, short-term variations in concentrations are not well characterized. Studies using real-time measurements of particles have demonstrated that concentrations of particles and specific components such as polyaromatic hydrocarbons (PAHs) have temporal and spatial variability associated with being close to ambient sources such as diesel emissions at roadways (*39,40*), and with a variety of household activities such as cooking and vacuuming, as well as being a function of air exchange rate (*41,42*). A study of indoor air concentrations of emissions associated with cigarette smoke found large gradients in air concentrations of particles within a room as cigarettes were smoked (*43*). The existence of short-term variations in air toxics occurs when individuals are in close proximity to localized sources or within indoor settings that have active emission sources. Thus, peak exposure excursions occur that are several times higher than the concentration measured in integrated samples over 12–48 hr. If brief exposures to high concentrations are important in the exacerbation or causation of asthma, many of the existing sampling protocols and exposure studies do not adequately define those exposures.

Population-Based Air Toxics Exposure Studies

A series of studies called the the Total Exposure Assessment Methodology (TEAM) Study were conducted between 1979 and 1985 to determine exposure to air toxics on a population basis and to assess the influence of ambient sources on that exposure (*44*). The TEAM study goals were to develop methods to measure total exposure of individuals via air, water, and food and the resulting body burden from exposure and to apply those methods, within a probabilistic-based sampling framework, to measure air toxics exposure in several U.S. cities. No health data on asthma were collected during the TEAM study, so it is not possible to establish from the TEAM studies whether exposure to air toxics affected asthmatic individuals. However, the TEAM and other exposure studies can be used to establish where air toxics exposures occur and the source of those air toxics. This information can be used to evaluate the role of ambient air toxic emissions on exposure and, for those air toxics documented to adversely affect asthmatic individuals, whether ambient emissions are potentially important contributors to exacerbation or causation of asthma.

VOC Exposures

The original scope of the TEAM study included evaluation of four groups of chemicals that included different types of air toxics: VOCs, semivolatile organic compounds (pesticides and polychlorinated biphenyls), metals, and PAHs. Because, in 1979, the most comprehensive sampling and measurement methodologies existed for the VOCs, that group of compounds was the focus of the initial TEAM study. VOCs were measured in personal air, fixed-site air, and in breath and water samples in New Jersey, California, North Carolina, and North Dakota. Paired 12-hr personal air and outdoor air samples, one during the day and a second during the night, were collected. Although it has not been definitively demonstrated that the individual VOCs measured affect asthmatic individuals, the total loading of VOCs indoors, as discussed above, has been found to exacerbate asthma when the indoor air quality is poor. The relative importance of ambient and indoor exposures and sources of the VOCs and other air toxics should be considered in any plan to reduce emissions for compounds thought to exacerbate asthma.

To illustrate how exposure to HAPs varies by microenvironment and region, the weighted estimates or median values of the personal air concentrations are presented in

Table 1. Urban New Jersey weighted mean estimate of population estimate of air concentration (μg/m³).[a]

	Fall 1981		Summer 1982		Winter 1983	
	Personal air	Outdoor air	Personal air	Outdoor air	Personal air	Outdoor air
1,1,1-Trichloroethane	97	7.0	67	12	45	1.7
m,p-Dichlorobenzene	45	1.7	50	1.3	71	1.2
m,p-Xylene	52	11	37	10	36	9.4
Tetrachloroethylene	45	6.0	11	6.2	28	4.2
Benzene	28	9.1	NA	NA	NA	NA
Ethylbenzene	10	4.0	9.2	3.2	12	3.8
o-Xylene	16	4.0	12	3.6	13	3.6
Trichloroethylene	13	2.2	6.3	7.8	4.6	0.4
Chloroform	8.0	1.4	4.3	13	4.0	0.3
Styrene	8.9	0.9	2.1	0.7	2.4	0.7
Carbon tetrachloride	9.3	1.1	1.0	1.0	ND	ND

Abbreviations: NA, not analyzed; ND, not detected. [a]Data from U.S. EPA (*87,88*).

Table 2. Urban California weighted mean estimate of population estimate of air concentration (μg/m³).[a]

	Los Angeles, Feb 1984		Los Angeles, May 1982		Contra Costa, June 1984	
	Personal air	Outdoor air	Personal air	Outdoor air	Personal air	Outdoor air
1,1,1-Trichloroethane	69	7.0	67	12	45	1.7
m,p-Dichlorobenzene	28	1.7	50	1.3	71	1.2
m,p-Xylene	18	11	37	10	36	9.4
Tetrachloroethylene	16	6.0	11	6.2	28	4.2
Benzene	18	9.1	NA	NA	NA	NA
Ethylbenzene	11	4.0	9.2	3.2	12	3.8
o-Xylene	13	4.0	12	3.6	13	3.6
Trichloroethylene	7.8	2.2	6.3	7.8	4.6	0.4
Chloroform	1.9	1.4	4.3	13	4.0	0.3
Styrene	3.6	0.9	2.1	0.7	2.4	0.7
Carbon tetrachloride	1.0	1.1	1.0	1.0	ND	ND
n-Octane	5.8	3.9	4.3	1.7	2.3	0.5
n-Decane	5.8	3.0	3.5	0.7	2.0	3.8
n-Undecane	5.2	2.2	4.2	1.0	2.7	0.4
n-Dodecane	2.5	0.7	2.1	0.7	2.1	0.2
α-Pinene	4.1	0.8	6.5	0.5	2.1	0.1
1,2-Dichloroethane	0.5	0.2	0.1	0.06	0.1	0.5
p-Dioxane	0.5	0.4	1.8	0.2	0.2	0.1
o-Dichlorobenzene	0.4	0.2	0.33	0.1	0.6	0.07

Abbreviations: NA, not analyzed; ND, not detected. [a]Data from U.S. EPA (*87,88*).

Table 3. Suburban/rural weighted mean estimate of population estimate of air concentration (μg/m³).[a]

	Greensboro, NC		Devils Lake , ND	
	Overnight personal air	Outdoor air	Overnight personal air	Outdoor air
1,1,1-Trichloroethane	26	60	37	0.05[b]
m,p-Dichlorobenzene	3.4	0.4	1.7	0.07[b]
m,p-Xylene	6.4	1.5	8.4	0.05[b]
Tetrachloroethylene	2.8	0.7	4.4	0.69
Benzene	11	0.4	NR	NR
Ethylbenzene	2.2	0.3	2.8	0.03[b]
o-Xylene	3.7	0.6	3.5	0.05[b]
Trichloroethylene	1.0	0.2	0.7	0.08[b]
Chloroform	2.3	0.14	0.14	0.05[b]
Styrene	0.8	0.1	NR	NR
Carbon tetrachloride	1.3	0.1	0.8	0.46[b]

Abbreviations: NR, not reported. [a]Data from U.S. EPA (*87,88*). [b]Not detected; value given is one-half the detection limit.

Table 4. Air concentrations measured during Arizona NHEXAS study (μg/m³).[a]

	Indoor air				Outdoor air				Indoor/ outdoor ratio
	Median	75%	90%	Max	Median	75%	90%	Max	
Benzene	1.3	4.0	9.5	90	1.0	2.0	3.6	9.0	1.3
Toluene	10	22	49	368	2.2	5.1	11	19	4.6
Trichloroethylene	<1.8	<1.8	<1.8	24	<1.8	<1.8	<1.8	< 1.8	—
Formaldehyde	21	21	34	40	6.3	13	25	61	3.3
1,3-Butadiene	<0.38	<0.38	<0.38	0.6	<0.38	<0.38	<0.38	<0.38	—

[a]Data from Gordon et al. (*50*).

Tables 1–3. The overall pattern observed for the VOCs is similar to that of many but not all HAPs. The median values of the personal air concentrations exceeded those in outdoor air during all seasons for nearly all compounds in urban centers in New Jersey and California, in a suburban community in North Carolina, and in a rural area of North Dakota (Tables 1–3). Estimated frequency distribution plots prepared for each compound showed that the personal air concentrations were predicted to exceed the outdoor air concentrations during both the day and night for all the air toxics across the majority of the population in each study area (*44–48*). The observation that the personal and indoor exposures exceeded—often greatly—the outdoor VOC air toxic concentrations was a major finding of the TEAM study. This led to the "conclusion that indoor air in the home and at work far outweighs outdoor air as a route of exposure to these chemicals" (*44*).

A major reason for the observed differentials between personal/indoor air concentrations and outdoor air concentrations in the TEAM and subsequent studies is the close proximity of individuals to small emissions in different locations and during different activities combined with the limited volume of indoor environments compared with the dilution that occurs outdoors. Emissions within enclosed spaces result in higher indoor and personal concentrations than in outdoor concentrations even though the mass of emissions of the air toxics to the ambient air is much greater. In addition to collecting air samples, the TEAM study included a questionnaire that was completed by each participant regarding his or her activities and duration spent in different locations. Stepwise regression analyses were conducted for each compound to attempt to evaluate specific activities or locations that could have contributed to the observed exposures. Specific sources of exposures identified included smoking (aromatic compounds); use of hot chlorinated water (chloroform); use of air fresheners, deodorizers, or moth crystals (*p*-dichlorobenzene); and travel by and refueling an automobile (aromatic compounds). The TEAM studies clearly indicated that exposures to volatile organic air toxics occur in places other than outdoors and that sources of volatile organic air toxics other than ambient emissions contribute significantly to exposure.

A more recent probabilistic population-based study to assess the U.S. nationwide exposure to multiple contaminants, including air toxics, is the National Human Exposure Assessment Survey (NHEXAS) (*49*). A feasibility pilot was conducted in three location: U.S. Environmental Protection Agency (U.S. EPA) Region 5 (Midwest); Arizona; and Baltimore, Maryland. Results reported for

VOCs in Arizona were similar to those found during the TEAM study (*50*). The concentrations were typically log-normally distributed, with indoor concentrations higher than outdoor concentrations (Table 4). Besides environmental tobacco smoke, having an attached garage, and use of spot remover and cleaning solvents were identified as sources of volatile organic air toxics in the U.S. EPA Region 5 portion of NHEXAS (*51*).

PM Exposure

Many of the air toxics listed as HAPs are attached to PM (e.g., metals, semivolatile and nonvolatile organic compounds, VOCs, and pesticides). PM, in the form of environmental tobacco smoke and diesel emissions, has been suggested as an environmental trigger of asthma, although it has not been confirmed whether it is the PM or the individual components present, such as the air toxics, that exacerbate asthma. The mechanisms that control the production and transport of particles differ from those of VOCs. The particle size range of the air toxics is important when investigators consider whether a particle will penetrate into the lung when inhaled and its lifetime within and transport through different microenvironments. Particles less than 10 μm can be inhaled, with various cutoff size fractions examined in different studies. Wallace (*52*) summarized three major U.S. studies conducted to understand population-based exposure to PM. These are the Harvard Six-Cities Study conducted between 1979 and 1988 that made measurements in 1,400 homes (*53*), the New York State Energy Resources and Development Authority (ERDA) study conducted in 1986 in 433 homes,(*54*) and the Particle TEAM (PTEAM) study conducted in 1990 in 178 homes (*55–57*). Within the Harvard Six-Cities Study, the mean mass concentration of particles below 3.5 μm was higher in the indoor air than in the outdoor air in five of the six cities. The major source of indoor PM was cigarette smoke, contributing more than 25 $\mu g/m^3$ additional mass to the indoor air (*58*). As indicated previously, environmental tobacco smoke is an environmental trigger of asthma. The source contributions of the indoor PM were reconstructed using principal component and linear regression analyses of the elemental data, measured by X-ray fluorescence analysis. Soil, wood smoke, sulfur-related particles, mobile emissions, indoor dust, industrial emissions (steel and iron), and an unexplained component contributed to the indoor air concentration of PM. The proportion associated with each source varied with the sample being collected from a smoker versus nonsmoker home or outdoors versus indoors and with season. Ambient particles penetrate indoors, but deposition of particles occurs, with greater losses for larger particles (*59*). In nonsmoker homes the ratios of indoor to outdoor air concentrations of PM mass during the summer were near 1.0, whereas in the winter they were higher (1.04–1.4) depending on the city. Similar results were obtained from the ERDA study, with the indoor particulate matter having a mass median aerodynamic diameter less than 2.5 μm ($PM_{2.5}$), approximately double the outdoor concentrations, and smoking increasing the indoor concentration [Sheldon et al. (*54*) as reported by Wallace (*52*). The ERDA study focused on different combustion sources in the home and found that, besides smoking, only kerosene heaters elevated indoor PM levels. Wood stove/fireplace and gas stove use did not have a significant effect on the indoor PM air concentration.

Although total mass of particles is not classified as an air toxic, PM contains air toxics. Transport phenomenon governing total mass will also apply to the particulate air toxics of the same size range. A knowledge of the sources contributing to production and the transport of PM is therefore important in understanding exposure to air toxics. Further, particle loading and chemical irritants contained on the surface of particles may affect asthmatic individuals differently, so source contributions should be considered in epidemiologic studies of asthma.

Wallace (*52*) used the PTEAM data to calculate the fraction of outdoor particles found indoors at equilibrium. He estimated that the fraction of outdoor fine particles ($PM_{2.5}$) in indoor air was 0.7 ± 0.2, with an expected range from 0.3 to 0.95 and 25th, 50th, and 75th percentiles of 0.6, 0.7, and 0.8, respectively. The fraction of outdoor PM_{10} (particulate matter with a mass median aerodynamic diameter less than 10 μm) entering the home was approximately 20% less than that for the fine particles. The fraction of particles that actually infiltrate into an individual home is a function of their deposition rate and removal processes as the air infiltrates into the home. In addition, air exchange rate can alter the proportion of the indoor particle concentration associated with ambient sources because higher air exchange rates typically increase infiltration rates and decrease the buildup of PM from indoor sources. Lower air exchange rates and tighter homes would lower the proportion of particles in the home from outdoor sources. Personal air concentrations of particulate air toxics are often higher than the outdoor levels, resulting in higher exposures than what is measured at outdoor monitoring stations. The concentration of PM air toxics attributed to ambient derived PM would then be lower than outdoor concentrations, particularly for air toxics on larger particles, even though the total exposure is greater.

Speciation of PM

PM sources associated with combustion and resuspension are expected to increase the indoor and personal air concentrations of not only PM mass but also air toxics. Cigarette smoke and other combustion processes produce particles containing PAHs and metals that are classified as HAPs. Resuspended dust will include a combination of deposited ambient aerosols and particles generated by activities that can mobilize heavy metals (e.g., lead from paint or tracked in from soil) (*60*), PAHs (*61*), and pesticides from residential or outdoor applications (*62,63*). These indoor processes contribute to particulate air toxics exposures. For example, smoking, construction, cleaning (sweeping, vacuuming, dusting), and use of combustion sources were factors contributing to indoor air particulate concentrations and individual air toxic metal concentrations (lead, arsenic, and cadmium) in the NHEXAS U.S. EPA Region 5 study (*51*). A number of other recent studies have collected samples that are expected to provide data on particulate air toxics [Air Pollution Exposure Distributions of Adult Urban Populations in Europe (EXPOLIS) (*64*), The Relationship of Indoor, Outdoor and Personal Air (RIOPA) study, and the TEACH (Toxic Exposure Assessment, a Columbia/Harvard) study (*65*). These studies have included measurements of a range of air toxics in indoor, outdoor, and personal air.

The ranges of air concentrations of the pesticides measured during NHEXAS in Arizona were higher indoors (chlorpyrifos < 3.2–3,280 ng/m^3, diazinon < 2.1–20,500 ng/m^3) than outdoors (chlorpyrifos < 3.2–22.5 ng/m^3, diazinon < 2.1–131 ng/m^3). Pesticides in indoor air result not only from the direct emissions during application but also from evaporation into the air from applied surfaces or resuspension of particles on which pesticides are deposited. Summary data presented by Gordon et al. (*50*) had consistent ranges and median concentrations across different seasons in Florida, Massachusetts, and Texas. Thus, as was found for the VOCs, air toxic pesticide exposures are elevated because of their use indoors.

Carbonyl Exposures

Some carbonyl compounds are respiratory irritants (*66*), including formaldehyde and acetaldehyde, the two most frequently measured aldehydes (*67*). Formaldehyde, acetaldehyde, and acrolein ambient air concentrations were modeled in the Cumulative Exposure Project based on ambient emissions. The Cumulative Exposure Project was undertaken by the U.S. EPA to estimate exposure to outdoor air concentrations for a large portion of the HAPs using emission rate data and information on populations

from individual census tracts (*68*). The calculated ambient air concentrations were above levels set to protect the population from a potential health risk (*10*). In addition to the outdoor emissions, formaldehyde and acetaldehyde have multiple indoor sources from off-gassing of common materials and glues used in construction and furnishings (*69*). Paired indoor and outdoor air concentrations of nine aldehydes, including formaldehyde and acetaldehyde, from samples taken in New Jersey homes showed that the indoor air concentrations exceeded the outdoor levels for all compounds except propionaldehyde, indicative of indoor sources (*67*). The mean ± standard deviation, 75th percentile, and maximum indoor and outdoor air concentrations for formaldehyde were 55 ± 20, 67, and 102 ppb and 13 ± 9, 20, and 34 ppb, respectively, whereas for acetaldehyde they were 3.0 ± 2.7, 3.3, and 16 ppb and 2.6 ± 2.3, 2.6, and 13 ppb, respectively. The mean indoor-to-outdoor ratios for formaldehyde and acetaldehyde were 7.2 ± 5.9 and 1.4 ± 0.9, respectively. These ratios confirm that indoor sources exist for these compounds and that indoor sources dominated the indoor formaldehyde air concentration. Reliable data have not been published on indoor air concentrations of acrolein because the standard aldehyde collection method for air samples using 2,4-dinitrophenylhydrazine–coated sorbents is not stable for acrolein. A recent passive sampling method using 5-dimethylaminonaphthalene-1-sulfohydrazide–coated sorbents appears to collect and stabilize acrolein adequately (*70*). This sampler was used in the RIOPA study, and evaluation of indoor exposure to acrolein and other aldehydes from that study should be available in the near future.

In-Vehicle Air Concentrations

Traveling in automobiles and on other modes of transportation, or even being near roadways, can result in increased air toxics exposures for compounds emitted by mobile sources (*71*). Mean concentrations of benzene, toluene, and other aromatic air toxics in the cabins of automobiles and public transportation and near roadways exceed both indoor and ambient air concentrations (*72–76*). Even higher concentrations have been measured for individuals riding motorcycles or bicycles in or near traffic (*77,78*). Measurements of PM and formaldehyde are also elevated in these microenvironments compared with indoor or ambient outdoor levels (*76,79,80*).

Activity Pattern Data

To comprehend the importance of examining exposure to air toxics arising from nonambient emissions, it has to be recognized that people spend the majority of their time indoors and only a small fraction of their time outdoors. One caveat to using solely the time spent in different microenvironments when considering the role of exposure to air pollutants in asthma is that physical exertion alters the dose delivered to the lungs, and more physical activity is done outdoors. Physical exertion may be important in asthma exacerbation. Numerous time–activity studies have been compiled and summarized in the U.S. EPA *Exposure Factors Handbook* (*81*). The data in the *Exposure Factors Handbook* have been grouped by age and gender and across many activities and locations. More recently, the National Human Activity Pattern Survey (NHAPS), a 2-year probability-based telephone survey, was conducted by the U.S. EPA to provide a resource for assessing exposure to environmental pollutants (*82,83*). The NHAPS data set indicates that nationwide the breakdown of time in different locations for the entire U.S. population is, in a residence, 68.7%; indoors in an office/factory, 5.4%; indoors in a bar/restaurant, 1.8%; other indoor locations, 11%; in a vehicle, 5.5%; and outdoors, 7.6%. Some variations in percentages occur for different age groups, times of the year, and regions of the country. These variations can be important when trying to understand whether a particular exposure is affecting a potentially sensitive subgroup.

As suggested above, physical activity can affect exposure and dose, exacerbating asthma if environmental triggers are present in the air being breathed because higher levels of physical activity increase the breathing rate and the potential dose delivered to the lungs. Further, the location of physical activity may be preferentially outside, especially for children, and may occur during specific times of the year. Estimates of physical activity level and duration while outside, stratified by age, season, and gender, have been compiled based on questionnaire data (*82,83*). The highest level of outdoor activity occurs for yard work/maintenance in the spring during morning to early afternoon and for sports/exercise in the summer (3–6% of respondents) during the middle of the day from noon to 3 PM. The time period for sports/exercise in the spring (5% of respondents) was from 3:30 to 6 PM. Outdoor activities also vary between weekends and weekdays: weekend activity tends to be throughout the day (9 to 5 PM), whereas during weekdays the time when physical activity occurs outdoors is shifted to later in the day, with an initial rise at 3 PM that extends into the evening. These differences reflect the time periods during which people have leisure time. Klepeis et al. (*82,83*) also reported differences in the amount of time that different age groups spent in various activities, with school-age children spending more time at sports/exercise than other age groups. The numbers of hours that healthy, asthmatic, and wheezy children spent outdoors during the spring and summer were similar (*84*). However, the amount of time asthmatic children spent being physically active outdoors was smaller than that for the healthy or wheezy children, particularly during the summer. Girls spent less time outdoors and were less physically active than boys. Overall, having an estimate of the number of hours in different microenvironments and how many of those hours were engaged in physical activity will improve inhalation exposure estimates in epidemiologic studies of asthma and air pollution.

Long-Term Temporal Trends

NHEXAS is the first nationwide U.S. population–based exposure study designed with a conceptual component to examine seasonal

Table 5. HAP air concentration measurements from Camden, New Jersey (μg/m^3).[a]

	Measured 1990 air concentration	Measured 1997 air concentration	Percentage change in air concentration
Benzene	4.3	1.8	–58
Bromoform	0.0	0.0	NA
1,3-Butadiene	0.22	0.16	–31
Carbon tetrachloride	1.1	0.80	–53
Chlorobenzene	0.56	0.046	–18
Chloroform	0.0	0.00	NA
Chloroprene	0.37	0.11	–71
Ethylbenzene	1.1	0.62	–41
Hexane	NA	2.0	NA
Methylene chloride	2.4	0.31	–87
Styrene	NA	0.10	NA
Tetrachloroethane	0.39	0.007	–98
Tetrachloroethylene	3.5	0.31	–83
1,1,2-Trichloroethane	0.15	0.11	–26
Trichloroethylene	0.38	0.030	–92
Toluene	8.5	4.9	–42
Xylenes	5.5	2.0	–64
Vinyl chloride[b]	1.8	0.26	–86

[a]Data from New Jersey Department of Environmental Protection (*89*). [b]Analytical problem makes 1990 value suspect.

and long-term temporal exposure trends (*49*). The first phase of NHEXAS evaluated the feasibility of the approach and methodologies. Subsequent phases of NHEXAS, pending approval of funding, will include collection of multiple years of data. If the full NHEXAS project is undertaken, a wealth of information on spatial and temporal exposures to air toxics will be gathered. The NHEXAS exposure database will provide the opportunity for establishing associations between health outcome data collected by state health agencies on asthma, and exposure to air toxics. NHEXAS should also provide insights into which sources contribute most to that association.

Seasonal trends for 26 VOCs, which included aromatic and chlorinated air toxics, were examined in a Canadian study that collected 24-hr average indoor air samples in 754 residences using a passive monitoring technique (*85*). It employed a probabilistic sampling design with both weekday and weekend sampling. Seasonal differences were observed for the average VOC indoor air concentrations, with the spring and fall having higher average concentrations than the winter and summer. However, not all compounds followed this pattern, suggesting differences among houses and activity patterns of the individuals affected by the air pollutant concentrations. The authors proposed that the use indoors of different products such as paints, fuels, and cleaners contributed to the variability in the seasonal pattern and the maximum concentrations measured. Outdoor temperature, indoor temperature, and indoor relative humidity were also significant variables that contributed to the variance in the air concentrations based on factor analysis. Air exchange rates were evaluated in a subset of homes and found to be lowest in the winter, intermediate in the spring, and highest in the summer and fall. The highest average concentrations were when the temperature and air exchange rates were the lowest.

To evaluate long-term temporal trends in the outdoor contribution of air toxics to exposure, data from ambient monitoring sites can be used. Although a national network of HAP monitoring sites has not been established, the photochemical assessment monitoring station (PAMS) network in 21 ozone nonattainment areas has collected data on ozone precursors, which include some of the volatile organic HAPs (*18*). The majority of the HAPs measured had statistically significant declines in annual mean concentrations for 1994 to 1995 and 1995 to 1996 at all sites (ethyl benzene, toluene, *m,p*-xylene, and *o*-xylene) or at all but one site (benzene, styrene, and 2,2,4-trimethylpentane). Hexane was the only compound that increased at two sites between 1994 and 1996 and was unchanged at the other sites (n = 3, 1994–1995; n = 4, 1995–1995). Several states have voluntary ambient air quality programs that include air toxics. The station in Camden, New Jersey, has been operated since 1990. Decreases in ambient air levels have been measured for all volatile organic HAPs (Table 5). These data suggest that exposure to volatile organic air toxics associated with ambient emissions has decreased during the 1990s. Although it is unclear if any of the HAPs individually, at ambient concentrations, exacerbate asthma, the combined VOC concentration may be a respiratory irritant. Long-term trends of PM_{10} have been reported because it is a criteria pollutant. Its concentration has been decreasing with time in most locations. Long-term trends of carbonyls and other air toxic respiratory irritants have not been reported.

Results from the RIOPA Study

The RIOPA study is a multicity, multipollutant study undertaken to evaluate the impact of ambient sources in urban settings on exposure. Homes close to ambient sources were

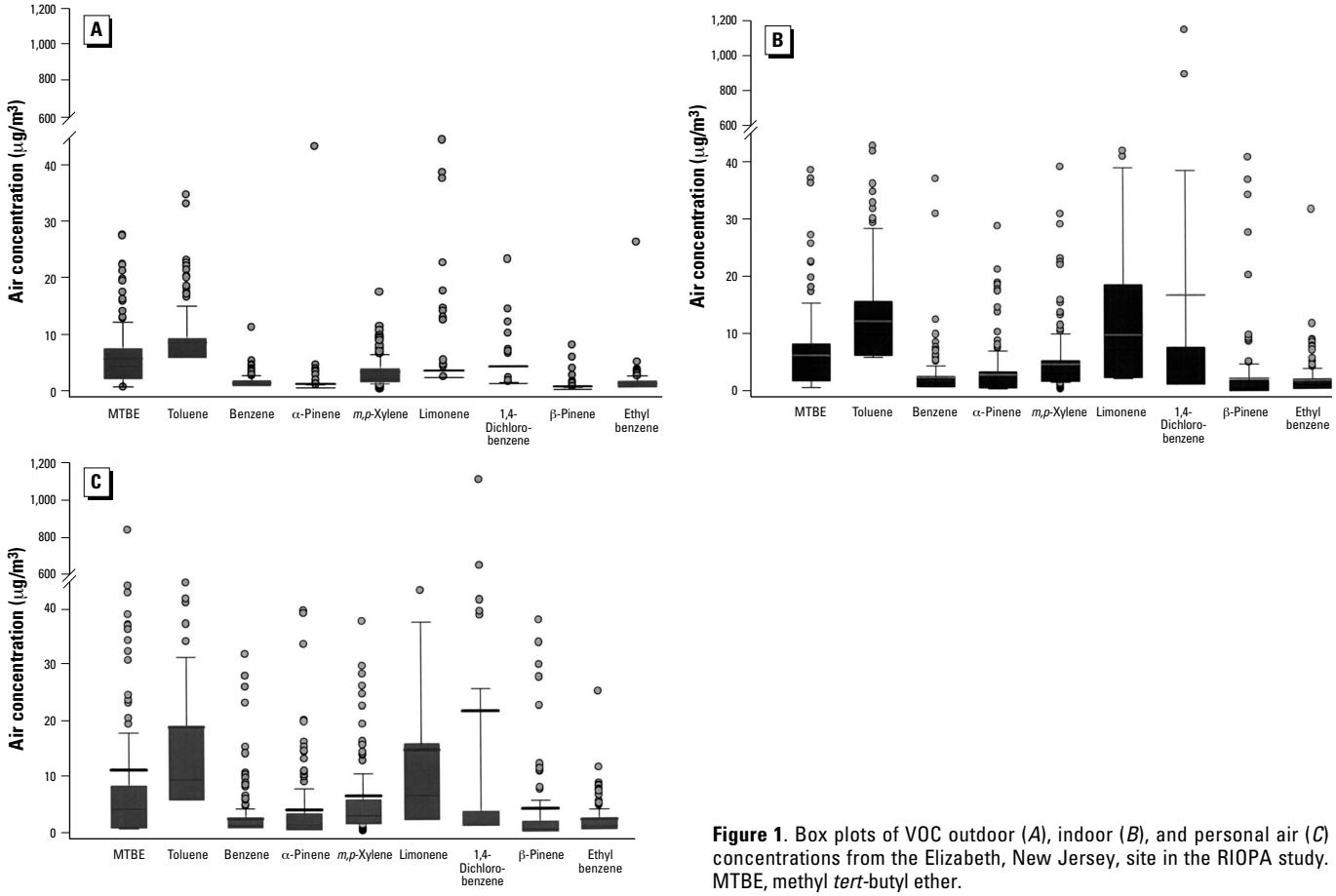

Figure 1. Box plots of VOC outdoor (*A*), indoor (*B*), and personal air (*C*) concentrations from the Elizabeth, New Jersey, site in the RIOPA study. MTBE, methyl *tert*-butyl ether.

oversampled during RIOPA. Only homes without smokers were included. Smoking elevates the indoor and personal air concentrations of many air toxics, and cigarette smoke is the dominant exposure source of many air toxics for smokers. Only the data on the indoor and outdoor air concentrations for VOCs in homes in Elizabeth, New Jersey, one of the cities sampled during RIOPA, are presented in this article. As discussed above, VOCs may have a role in exacerbation of asthma. Integrated 48-hr air samples were collected from 100 homes. Elizabeth, New Jersey, contains a mixture of mobile, commercial area, and industrial point sources. The 48-hr VOC samples were collected using passive monitors, a different method from that used when the two sequential 12-hr active samples were taken during the TEAM study, which also sampled in Elizabeth, New Jersey, for a similar suite of VOCs. However, the RIOPA project was not a probabilistic population-based study; rather, two-thirds of the homes were selected to be close to ambient source emissions.

Although many of the VOCs have mean, median, and upper outlier air concentrations in the indoor and personal samples that exceed those for outdoor air, others had VOC air concentrations that were similar (Figure 1). Thus, as was found during the TEAM study, indoor VOC sources and VOC sources close to people can contribute to inhalation exposure. The exclusion of homes with smokers from the RIOPA but not the TEAM study resulted in a smaller differential between indoor and outdoor mean and median concentrations of aromatic VOCs. The temporal pattern of many ambient air VOC concentrations shows spikes in the air concentrations on individual days over the 1.5 years that the samples were collected (Figures 2, 3). The concentrations for compounds with mobile sources were higher than those of chlorinated compounds with industrial or commercial sources. No obvious seasonal pattern was observed for either data set, which could reflect the varying sampling locations selected throughout the year rather than a true lack of seasonality in the air concentrations. The temporal pattern of the three chlorinated compounds shows two different patterns. Carbon-tetrachloride shows little variability throughout the year among the different locations where the samples were collected throughout the city, consistent with few ambient sources of this compound. Other chlorinated compounds, represented by tetrachloroethene and 1,4-dichlorobenzene, have periodic spikes in their ambient concentrations above a very low background concentration, which was typically at the detection limits of the method. Such spikes suggest individual releases of these compounds from ambient sources either near the sampling location or within the urban settings, or under meteorological conditions that enhance the buildup of concentrations from a constant release.

The relative importance of ambient sources on indoor air concentrations for different compounds can be observed in the scatter plots of indoor versus outdoor air concentrations of the New Jersey RIOPA data. Data for five example compounds, methyl *tert*-butyl ether, benzene, toluene, 1,4-dichlorobenzene, and carbon tetrachloroethane, are provided here (Figures 4–8). These compounds were selected because they have potentially different contributions to indoor air and exposure by ambient sources and indoor sources. Mobile emissions are the major ambient air sources for methyl *tert*-butyl ether, benzene, and toluene. Few other ambient emissions or indoor sources exist for methyl *tert*-butyl ether. Although benzene is contained in cigarette smoke, which should not be present in the vast majority of the samples collected because of the exclusion criteria

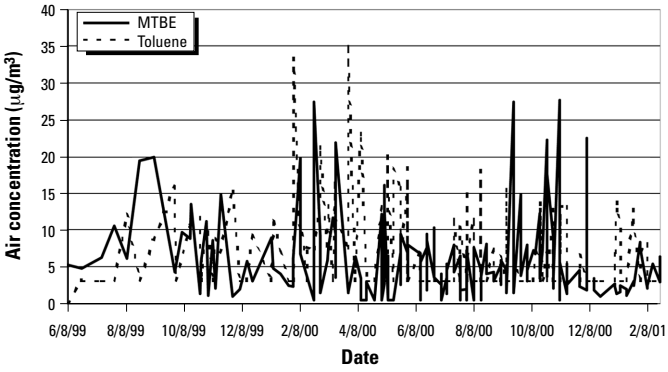

Figure 2. Temporal air concentration of selected mobile source compounds [methyl *tert*-butyl ether (MTBE), and toluene] from the Elizabeth, New Jersey, site in the RIOPA study.

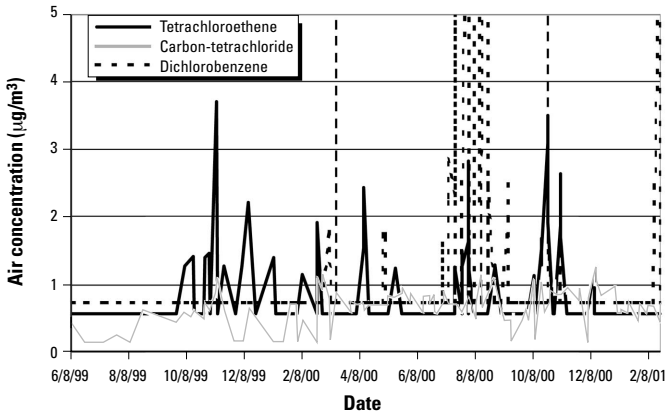

Figure 3. Temporal air concentration of selected chlorinated compounds (tetrachloroethene, carbon tetrachloride, and 1,4-dichlorobenzene) from the Elizabeth, New Jersey, site in the RIOPA study.

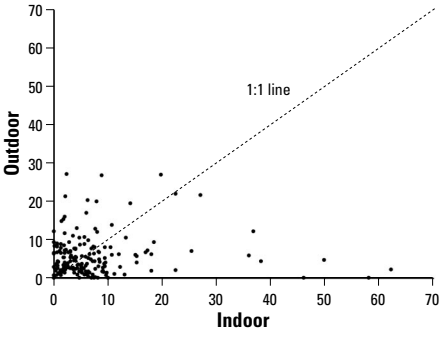

Figure 4. Scatter plot of the outdoor and indoor air concentrations (μg/m^3) of methyl *tert*-butyl ether (MTBE) from the Elizabeth, New Jersey, site in the RIOPA study.

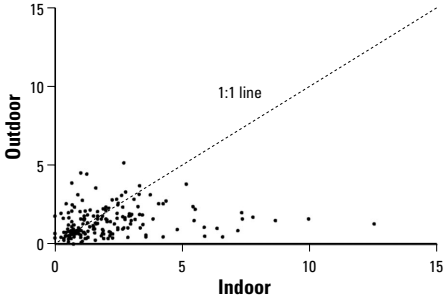

Figure 5. Scatter plot of the outdoor and indoor air concentrations (μg/m^3) of benzene from the Elizabeth, New Jersey, site in the RIOPA study.

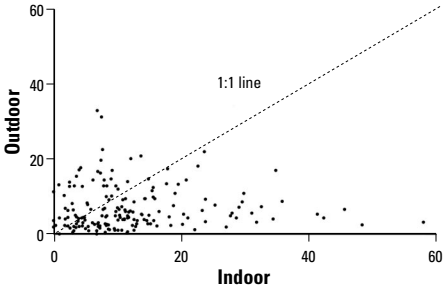

Figure 6. Scatter plot of the outdoor and indoor air concentrations (μg/m^3) of toluene from the Elizabeth, New Jersey, site in the RIOPA study.

of the RIOPA study; the use of benzene in most personal and household products has been banned and is limited in industrial and commercial settings. Toluene is a component of cigarette smoke and used as a solvent in personal, household, commercial, and industrial products. These differences are reflected in the scatter plots of each compound (Figures 4–6). Each compound has general scatter around the 1:1 line at the lower end of the concentration range. The scatters of the benzene and toluene data pairs are biased to slightly higher indoor air concentrations, whereas the methyl *tert*-butyl ether data are more equally distributed. At the higher concentration range, the indoor benzene concentrations are higher than the outdoor concentrations, consistent with a subset of homes having indoor sources of benzene. Methyl *tert*-butyl ether also has several homes with higher indoor than outdoor concentrations, which was unexpected because none of the homes had attached garages, one of the few known sources of indoor methyl *tert*-butyl ether. It also had paired samples where the outdoor air concentrations exceeded the indoor concentrations. The outdoor level could be higher if the outdoor sampler was near a localized source of methyl *tert*-butyl ether such as evaporative emissions from a car parked near the outdoor samplers, sometimes located in driveways. Toluene shows the greatest amount of variability, consistent with the larger number of ambient and indoor sources of toluene than of the other compounds.

The two chlorinated compounds selected show distinctly different patterns that can be explained based on known emission sources. Carbon-tetrachloride has few current uses and a fairly narrow range of indoor and outdoor concentrations, with values near the global background levels of less than 1 μg/m^3 (Figure 7). The data are distributed around the 1:1 line, with more points having higher outdoor than indoor concentrations, possibly caused by sinks in homes, such as absorption of the compound by the padding in furniture. Eleven homes have higher indoor values, suggesting the presence of carbon-tetrachloride in some product used in those homes. The scatter plots of 1,4-dichlorobenzene are consistent with a compound having minimal outdoor sources and large indoor sources (Figure 8). This compound had some of the highest indoor air concentrations measured for any VOC during the study, consistent with its use as a room air deodorizer and a major component of moth cakes [e.g., Wallace (*86*)]. If compounds present in deodorizers, such as dichlorobenzene, limonene, or pinenes, are respiratory irritants, the elevated exposure that occurs indoors may be a trigger for asthma, and controlling ambient sources of these compounds will not be effective in reducing exposure to them. It is therefore evident that although there is a major contribution to air toxics exposures from ambient emissions because these compounds penetrate into homes where people spend the majority of their time, other sources also contribute and exposure to each air toxic must be determined individually.

Conclusions

Asthma is a common respiratory disease whose prevalence is increasing. Many environmental triggers can exacerbate asthma and could include nonspecific responses to HAPs. Inhalation exposure to air toxics occurs in multiple microenvironments, with the major source contributions varying by the air toxic, but the majority of the exposure occurs indoors. It may be important to consider different activity patterns and where those occur, particularly those related to physical exercise, because increased breathing rates increase the dose delivered to the lungs. Ambient emissions are transported through the environment and into houses. However, many air toxics have air concentrations higher indoors than outdoors and even higher in personal samples collected near the breathing zone. This is because the sources of air toxics within homes, even though they are small compared with ambient emissions, can contribute greatly to exposure because of the proximity of the source to the receptor, that is, people. In establishing whether an air toxic is associated with asthma exacerbation or causation, it is necessary to determine where the exposure occurs, the duration of exposure in each location, and the activities the individuals are involved in and not to assume that ambient measurements adequately define the exposure. The total concentration of multiple HAPs, rather than the concentration of individual compounds, may be important. These considerations, along with the source of the exposures, need to be included in any attempt to reduce exposure to protect the health of asthmatic individuals and any other population susceptible to air toxics exposures.

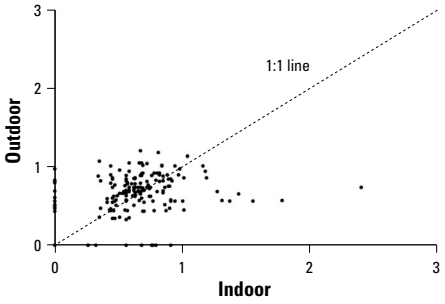

Figure 7. Scatter plot of the outdoor and indoor air concentrations (μg/m^3) of carbon-tetrachloride from the Elizabeth, New Jersey, site in the RIOPA study.

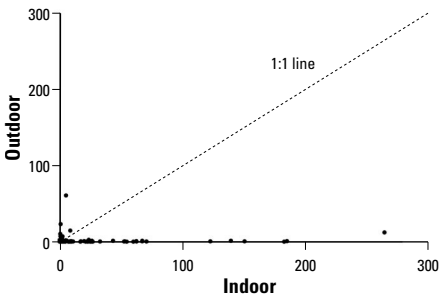

Figure 8. Scatter plot of the outdoor and indoor air concentrations (μg/m^3) of 1,4-dichlorobenzene from the Elizabeth, New Jersey, site in the RIOPA study.

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