Measurement Methods for Human Exposure Analysis

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The general methods used to complete measurements of human exposures are identified and illustrations are provided for the cases of indirect and direct methods used for exposure analysis. The application of the techniques for external measurements of exposure, microenvironmental and personal monitors, are placed in the context of the need to test hypotheses concerning the biological effects of concern. The linkage of external measurements to measurements made in biological fluids is explored for a suite of contaminants. This information is placed in the context of the scientific framework used to conduct exposure assessment. Examples are taken from research on volatile organics and for a large scale problem: hazardous waste sites. — Environ Health Perspect 103(Suppl 3):35-44 (1995)

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Introduction

Measurements and estimates of human contact with environmental contaminants involve the use of techniques that provide qualitative or quantitative data. Historically, approaches used to infer human exposures to a contaminant relied on information from general environmental quality measurements (1). Many of these techniques are prescribed for regulatory purposes. Thus, a sample taken in a water supply has been used as the basis for determining the exposure to chemicals in tap water, or an air sample taken on the rooftop of a building has been used to represent inhalation exposure to a chemical. During the late 1970s and early 1980s we began to realize that in many cases the approach was naive, if not wrong. Indoor air studies provided the most striking information to illustrate the error (2).

These demonstrated that for at least one route of entry to the body, inhalation, exposures to chemical products and by products could no longer be adequately predicted by an outdoor air monitor (3). In fact, it is now well established that for contaminants such as nitrogen dioxide, benzene, and carbon monoxide, outdoor exposures can be much lower, if not deminimus, compared to those which occur in other microenvironments (e.g., home or car). When nontraditional techniques and analyses are employed, similar types of observations can be made for contaminants present in other media. Two good examples of pollutant classes with nontraditional pathways of exposure are: a) volatile organic compounds present in shower water that can yield significant exposures by both the dermal and inhalation routes and b) contaminated soil (or dust) tracked into a home, and deposited on accessible surfaces which can be ingested by a child playing on or eating off the floor (4,5).

These types of observations have led to a reluctant acceptance of a paradigm that requires more accurate definition of human exposures, especially in situations that can lead to exposures that cause health effects. Some changes in sampling strategies have been made in epidemiology and risk characterization studies and now use currently available exposure measurement techniques (6,7). We have not, however, seen a dramatic increase in their utilization for regulatory surveillance. The 1992 U.S. EPA exposure guidelines have provided a serious attempt to mould a conceptual framework within the U.S. EPA's risk assessment program (8). The basic technology and theoretical framework are available for mounting a concerted effort to develop microenvironmental exposure and personal exposure monitors. Parallel efforts are being made to improve the population survey instruments and the statistical design used in studies (9). However, the resources necessary to conduct exposure methodology research are not readily available. These resources are needed because quantitative exposure data and exposure reduction analyses will improve risk assessment and the efficacy of control strategies (9).

A problem with the initial studies used to obtain exposure measurements was the lack of definite goals (9). Techniques and equipment were primarily employed for hypothesis generation rather than hypothesis testing studies. A paradigm for exposure assessment (Figure 1) was presented by the National Research Council (NRC) in 1991. Concurrently, interest in the role the exposure analyses play in health studies and risk characterization has shifted research efforts toward hypothesis testing types of experiments. Included could be measurements in the media containing the contaminant through to measurements of the biologically effective dose (9). This would also have the benefit of providing new opportunities to discover new methods to relate external exposure to an internal dose (biological markers), and opportunities to improve the theoretical basis of exposure analyses.

Methods for measuring and assessing exposure that may be adequate for an epidemiological study may not necessarily be the same as those required for a risk characterization. Depending upon the detail required and logistics associated with obtaining a dataset on a large population, a survey instrument may be the metric of choice for collecting exposure data in some types of epidemiological studies. For risk characterization, quantitative measurements of exposure are essential to improve the
validity of exposure and hazard calculations and to reduce uncertainty in population risk calculations.

Based upon the above, the purpose of this manuscript is a) to identify the different types of external markers of exposure, b) to describe the rationale for obtaining measurements of external markers, and c) to illustrate how external and internal markers of exposure are linked through quantitative exposure–dose relationships.

General Concepts for Using Exposure Analysis Techniques

Using the preceding as a guide post, the total number and types of exposure measurement methods that can be employed in a study would be analogous to having a set of tools. Some or all of the tools may or may not be required to analyze a problem, but an assessor’s tool box should include some generic types of direct and indirect measures of exposure (Figure 2). One or more could be given serious consideration for use in a specific study. Included as direct methods within the tool box are biological markers of exposure. These can play an important role in a) determining if an exposure has actually occurred, and b) measuring the magnitude of an individual’s current or accumulated internal dose. Much has been written on the potential utility of biological markers (measurements in fluids and tissues). However, we still have a limited set of validated techniques for use among the general population (7,10–12). The prospects for continued improvements are promising but are dependent upon validating the markers and establishing the baseline levels for markers within the general population.

If the preceding milestones are achieved, there have been suggestions that biological markers can be used as primary metrics of exposure. This is not an accurate statement because most biological markers can only tell you that a person has been exposed to toxicant and can possibly provide you with some quantitative data concerning when an exposure occurred (9). In situations limited to a single medium with low baseline contributions and within an isolated location (e.g., specific occupational task), biological marker data may be the only quantitative measurement necessary. However, these conditions are not always met. Thus, there is a need for continued development of external markers of exposure, which can be employed to a) quantify the increment of exposure derived from particular sources or media and b) identify the strategies necessary for exposure reduction and source control. This link-age, as shown in Figure 3, is essential to ensure that we can adequately address current and potential public health issues.

The techniques available for measuring or estimating external exposures are associated with five basic types of direct and indirect tools: a) general fixed site monitoring (indirect); b) microenvironmental monitoring (indirect); c) personal monitoring (direct); d) survey instruments (indirect); e) exposure models (indirect).

Techniques 1 to 3 provide measurements that are made progressively closer to the individual (Table 1), with the net result being a reduction in the uncertainty of an exposure assessment (12). An important set of companion information is obtained by survey instruments (4). These qualitative or semiquantitative instruments provide data that couple individual or population time–activity patterns with quantitative measurements. In some epidemiological studies, however, survey data may be all that is required to make an initial assessment of potential contact with contaminants. Finally, exposure models can predict future exposures within a specific population/microenvironment or extend measurement data collected in one or more

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**Figure 1.** Contaminant sources and effects continuum (9).

**Figure 2.** Possible approaches for analysis of air contaminant exposures (NRC, 1991).
studies to estimate the potential exposure within large segments of the population.

A classic example of the concurrent development of an exposure database and models involves research on human contact with carbon monoxide in automobile cabins, and confined vehicle microenvironments (parking garages) (13). These studies show conclusively that the highest exposures to the general population most commonly occur in these situations and not simply in the ambient air.

If one is to determine the exposure for a pollutant in multiple media, the analyses must account for the variety of human activities that lead to contact (swimming, drinking, eating, showering). The number and types of measurements needed to adequately characterize the nature or distribution of the exposure could be quite high (14). This issue can be extremely difficult to resolve in a specific experiment because of complexities associated with providing comparable measurements of exposure for each route of entry into the body. The U.S. EPA has begun to internalize the concept of exposure measurements with the design of a National Human Exposure Assessment Study (NHEXAS) (15). The intent is to develop an approach that can be used for long-term measurement and assessment of exposure for chemicals in multiple media. The conceptual framework is derived from Figure 3 with an emphasis on the need to link the type and time of human contact with a contaminant to its concentration. For NHEXAS to obtain an adequate assessment within the general population, large numbers of individuals must be sampled to obtain a statistically representative distribution of exposure.

Problem definition for exposure analyses becomes simpler when the requirements for instrumentaion and analytical techniques are coupled to specific biological question(s). It is then possible to set priorities for sampling and analyses with a framework similar to that presented by the NRC report (Figure 2) and to define the sampling duration and frequency to the level of contact necessary to cause an acute or biological response (9).

The characteristics of particular environmental contaminants would provide the first level of information needed to define external or internal measurement techniques since there is usually toxicological, chemical and physical data available. Some degree of caution should be used in reviewing such information, because, for example, toxicological data obtained to satisfy industrial chemical safety or the Toxic Substances Control Act of 1976 (TOSCA) requirements for carcinogenesis or mutagenesis may not be sufficient to eliminate concern for acute neurological responses (headaches, dizziness, etc.) and developmental effects. In any case, a level of information is available for many contaminants that can be used to establish the time scales for developing either an external or internal exposure measurement program (16).

**Measurement Issues**

The general issues that confront development of personal or microenvironmental monitors for air pollutants are shown in Table 2. The requirements, however, may change significantly for a specific pollutant. For example, the technical problems surrounding personal monitoring of CO are much less complicated than those of semivolatile organic matter (SVOC) since the former is a single pollutant that is relatively non-reactive in ambient air. Furthermore, the concentrations of CO are usually much higher than SVOCs in many microenvironments which precludes many problems associated with detection limits and the sample size for SVOC (9).

**Table 1.** Hierarchy of exposure data or surrogates.

| Types of data                                      | Approximation to actual exposure |
|----------------------------------------------------|---------------------------------|
| 1. Quantified personal measurements.              | Best                            |
| 2. Quantified area or ambient measurements in the vicinity of the residence or other sites of activity. |                                |
| 3. Quantified surrogates of exposure (e.g., estimate of drinking water use). |                                |
| 4. Distance from site and duration of residence.  | Best                            |
| 5. Distance or duration of residence.             | Poorest                         |
| 6. Residence or employment in geographic area in reasonable proximity to site where exposure can be assumed. |                                |
| 7. Residence or employment in defined geographical area (e.g., a county) of the site. | Best                            |

**Table 2.** Analytical method selection.

| Factor                   | Ideal condition                                                                 |
|--------------------------|---------------------------------------------------------------------------------|
| Sensitivity              | Detects analytes at levels below those causing adverse health effects; sensitivity 0.1X; level of interest; range 0.1X–10X level of interest; precision and accuracy ±5%; easy and accurate calibration. |
| Selectivity              | No response to similar compounds that might be present simultaneously with the analyte of interest. |
| Rapidity                 | Short sampling and analysis times compared with biological response time or with significant changes in contaminant concentration; response time 90% in less than 30 sec; RS232 or equivalent output. |
| Comprehensiveness        | Sensitive to all contaminants that could result in adverse health effects.     |
| Portability              | Sampling and analysis device is rugged and can be worn without modifying the normal behavior of individual; low power consumption; battery operated; stabilization time less than 15 min; temperature range –20 to –40°C, humidity range 0 to 100%. |
| Cost                     | Cost of sampling and analysis is not prohibitive; inexpensive, readily available components; few consumables; low maintenance. |
For nonvolatile compounds present in surface dust, microenvironmental samples are available, but not personal samplers. Thus, microenvironmental monitoring currently provides the best opportunity for estimating exposure. Even in these less stringent sampling situations, e.g., few restrictions on sample mass, the techniques for sampling lead dust are not equivalent to those needed for pesticide residuals: the former is an element and the latter is an organic complex. Thus, in each case, consideration must be given to the type of sampling media and how a representative sample can be collected from a rug versus a bare surface. Neither has been adequately characterized to date (17).

All types of monitors do not have to be employed in a particular exposure study. However, external measurements that provide data which assist in identifying the sources and the routes of entry will be needed in studies that employ biological markers. Such a format helps define the criteria for selecting instruments needed to complete microenvironment or personal monitoring measurements and establish exposure and internal dose relationships. This is not a simple task, but such measurements will improve attempts to match exposure models and pharmacokinetic models (9,18,19).

A different type of measurement problem is illustrated in the attempts to define exposures to lead, and chromium (20,21). The elemental forms of Pb and Cr are easily measured in a variety of media and some can be accurately measured in blood or urine, respectively (22,23). These materials are found in a multitude of locations and many media are readily available for contact through ingestion and inhalation. This makes the measurement or estimation of the total exposure difficult. A further complication is associated with the fact that these two elements can be present within different compounds, and all are not equally bioavailable for absorption by target tissue or cells in the body (24).

**Lead Measurements**

Measurement of blood lead must be coupled to the duration (historical) of exposure since Pb is retained in the bone marrow and has a relatively long half-life in the body. This usually precludes simple identification of the cause or source of the internal dose (blood) of Pb. Pharmacokinetic models are available to predict the dose–response relationship between levels of lead in various media and the levels of Pb found in the blood (25). But for a group of children at risk because of high blood lead levels, a number of microenvironmental measurements, and possibly personal measurements are necessary to identify the major exposures accumulated incrementally from particular media, e.g., house dust or soil (9).

Since there can be site specific or microenvironment specific variation of the lead levels in a medium, the use of generic or baseline information from typical or other locations is usually not adequate for assessing individual exposure. For instance, a child living in a home that has lead in the paint on the walls would have a potential exposure to lead paint. However, this may mislead an investigator dealing with contact at a particular location if the paint is not flaking or readily accessible for ingestion. In such situations, the source of the child’s exposure could be the park adjacent to the neighborhood (and frequented by the family) that contains 1000 µg/g of lead in the surface dust. The contact in this case, could be derived from the lead that can be brought into the home on shoes and clothing. It can then be ingested from a child’s dirty hands. Alternatively, it can be inhaled via dust resuspended while the child is playing in the park.

One of the major problems associated with understanding the process of lead or any chemical exposure in a given situation is the need to use the correct methods to determine the process of exposure that is most important. Because Pb is found in multiple media, sampling strategies for each microenvironment will not necessarily be equivalent. For instance, a dust sample used to collect material from a carpet and a bare floor are not equivalent. A well constructed flat surface dust sampler will collect between 85 to 95% of the mass on the surface (21). In contrast, a vacuum sampler used to collect the mass embedded in a rug will collect variable amounts of mass based upon the operating parameters of the vacuum and how tightly the Pb is bound to the carpet.

A recent review of dust sampling emphasized the need for standardized methods to estimate exposure. For instance, a calibration of one vacuum sample indicated that particle <5 m are not collected by the device (26). This is a concern since it has been suspected that the smaller particles adhere more firmly to a hand or other skin surface. Our Childhood Lead Exposure Assessment and Reduction Study (CLEARs) takes both wipe and vacuum samples (27). As you can see from the data for 43 homes (Figure 4) the Pb distribution obtained by each technique is different. For area coverage, the carpets showed the highest value for µg/cm² of surface in the living room and bedroom and had a wider distribution of values. In contrast, the concentration (µg/s) distribution of Pb in the dust samples was similar for both techniques, (Figures 5). Because of the nature of particle deposition and human activities that redistribute lead dust, each type of data will be useful in defining patterns that may lead to highest contact, e.g., entry way versus bedroom. They may also reveal different Pb distributions at a specific location (e.g., bimodal).

![Figure 4: Frequency distribution of living room area lead concentration for vacuumed and wiped samples.](image)

![Figure 5: Lead concentration in dust (PbD) frequency distribution of living room and bedroom for vacuumed and wiped dust samples.](image)
Chromium Measurements

Another elemental contaminant, chromium, presents other problems because the chemical form of Cr is dependent upon factors that include the physical characteristics of the medium which contains the Cr residues. For instance, waste containing Cr that has a pH 8 is much more likely to have chromium in the form of Cr(III) (the carcinogenic valence state) than at pH 4 (28). Furthermore, the presence of soluble forms of Cr will increase the possibility of transformations from Cr(III) to Cr(VI) in a soil, indicating that analyses of microenvironmental or soil samples must consider the need for species measurements. There are some instances where having total Cr values is sufficient, e.g., for comparisons with Cr levels in urine and defining homes with high chromium (23). In the study by Liow et al. (21) the homes with high Cr were readily identified by the total chromium in surface dust. As shown in Table 3, the information could only be obtained if the sampler was quantitative for concentration (micrograms per gram) as well as surface coverage (micrograms per square centimeter). The concentrations of Cr per unit mass were different with the highest values found at the sites nearest large or heavily contaminated sites (100, 200, 300). Personal or microenvironmental air samples should be made and specified if the inhalation or dermal exposure to the more toxic forms of Cr are needed for risk assessments.

Activity Patterns

In contrast to the above, the measurements required to obtain inferences about the incidence of disease using exposure data may, in some instances, be much cruder than obtained by a personal monitor or biological marker. Some studies may require a focused (purposive) exposure study to identify sources, intensity of exposure or recommend appropriate techniques for mitigation (9).

For instance, exposures to multiple chemicals require many measurements to accurately define the exposure for all compounds which can potentially affect individuals. Initially, however, it would be wiser to employ a questionnaire that identifies the general activities and the sources which can lead to human contact. If these data prove appropriate for qualitative identification of locations or activities that lead to high level exposure or the median exposure, then mitigation measures could be identified for the particular problem. Tables 4 and 5 from Freeman et al. (30) illustrates the data typically available from questionnaires which focus on questions associated with activity and source patterns. The degree of detail is dependent upon the complexity of the source-receptor issues and the patience of the subject for providing information. Clearly, Table 5 requires either a diary or another method for identifying the time spent in a particular location.

Table 3. Hudson County chromium exposure study comparison of mean vacuum and wipe samples by site. (29)

| Site             | Vacuum dust | Wipe dust |
|------------------|-------------|-----------|
|                  | Level, ng/cm² | Concentration, µg/g | Level, ng/cm² | Concentration, µg/g |
| 100              | 2.3 ± 1.1 (2.0) | 112.6 ± 104.8 (88.8) | 47.3 ± 35.8 (35.9) | 115.7 ± 51.8 (104.1) |
| Nonsmokers (2)   | 2.3 ± 1.2 | 78.0 ± 51.1 | 21.0 ± 2.5 | 70.1 ± 14.2 |
| Smokers (4)      | 2.2 ± 1.3 | 129.9 ± 127.4 | 60.4 ± 39.0 | 102.6 ± 31.6 |
| 200              | 4.3 ± 1.5 (3.0) | 208.9 ± 121.0 (188.8) | 97.9 ± 70.5 (77.9) | 213.8 ± 57.4 (207.1) |
| 300              | 1.0 ± 0.1 (0.9) | 104.9 ± 24.2 (103.5) | 54.5 ± 50.6 (41.1) | 193.4 ± 107.2 (177.9) |
| 400              | 1.2 ± 1.1 (0.7) | 79.3 ± 67.3 (49.3) | 14.6 ± 8.0 (12.1) | 150.3 ± 95.9 (118.7) |
| 500              | 2.6 ± 1.3 (0.3) | 87.6 ± 125.9 (26.5) | 22.7 ± 19.8 (14.3) | 193.8 ± 191.0 (112.3) |
| Unrenovated      | 0.4 ± 0.7 (0.1) | 34.5 ± 48.5 (14.5) | 21.6 ± 22.7 (12.2) | 123.5 ± 111.4 (95.1) |
| 600              | 3.0 ± 1.0 (1.4) | 85.2 ± 61.5 (51.4) | 3.3 ± 0.0 (3.3) | 71.3 ± 44.9 (47.8) |
| Unrenovated      | 1.7 ± 1.6 (0.8) | 73.7 ± 70.9 (36.3) | 3.3 ± 0.0 (3.3) | 29.5 ± 19.0 (39.0) |

Comparison of mass and chromium levels by Hudson County sites (Kruskal–Wallis nonparametric analysis of variance)

| Floor mass, µg/cm² | p = 0.411 | n = 18 | df = 3 | Site 200 > 300, 400 |
| Floor Cr, µg/cm² | p = 0.089 | n = 18 | df = 3 | Site 400 < 300, 200, 100 |
| Floor concentration, µg/g | p = 0.146 | n = 18 | df = 3 | Site 200 > 300, 400 |
| Wipe mass | p = 0.121 | n = 18 | df = 3 | Site 200 > 300, 400 |
| Wipe Cr, µg/cm² | p = 0.035 | n = 18 | df = 3 | Site 400 < 300, 200, 100 |
| Wipe concentration, µg/g | p = 0.090 | n = 18 | df = 3 | Site 200 > 100 |

df = degree of freedom  Number of houses.  Numbers given are arithmetic mean ± SD. Numbers in parentheses are geometric mean.

Table 4. Total human environment exposure study (THEES): participant and household characteristics.

| PID  | Age | Sex | Occupation       | Age | Heat sources | Oven type |
|------|-----|-----|------------------|-----|--------------|-----------|
| 01   | 29  | M   | Graduate student | 61  | Oil          | Gas       |
| 02   | 56  | M   | Graduate student | 61  | Oil          | Gas       |
| 11   | 33  | F   | Retired          | 95  | Oil          | Gas       |
| 31   | 34  | F   | Part-time sales  | 80  | Oil, space heater | Electric |
| 41   | 49  | F   | Billing clerk   | 60  | Oil, space heater | Gas       |
| 51   | 74  | F   | Retired          | 75  | Oil          | Electric  |
| 52   | 79  | M   | Retired          | 61  | Oil          | Electric  |
| 61   | 36  | F   | Housewife        | 70  | Gas          | Electric  |
| 62   | 41  | M   | Fireman          | 65  | Oil          | Gas       |
| 81   | 27  | F   | Housewife        | 65  | Oil          | Gas       |
| 82   | 28  | M   | Chemist          | 100 | Oil, coal     | Gas       |
| 101  | 41  | F   | Office clerk     | 100 | Oil, coal     | Gas       |
| 102  | 44  | M   | Factory worker   | 100 | Oil, coal     | Gas       |

PID = person identification number in THEES.

Table 5. Summary of microenvironment use for participants in the total human environmental exposure study, January 1988.

| PID | Microenvironment mean use in hours |
|-----|-----------------------------------|
|     | Occupational status | Home | Work | Indoors | Outdoors | Travel |
| 01  | Student               | 14.1 | 1.5  | 3.1     | 16.6     | 3.0    |
| 02  | Student               | 9.2  | 4.7   | 5.9     | 1.2      | 3.0    |
| 11  | Retired               | 23.1 | 0.4   | 0.2     | 0.4      | 1.3    |
| 31  | Part-time             | 16.2 | 1.5   | 4.9     | 0.2      | 1.3    |
| 41  | Full-time             | 17.0 | 4.2   | 0.9     | 0.2      | 1.3    |
| 42  | Full-time             | 16.7 | 5.0   | 0.7     | 0.3      | 0.3    |
| 51  | Retired               | 21.4 | 0.8   | 0.6     | 0.3      | 0.3    |
| 61  | Housewife             | 21.4 | 0.7   | 0.6     | 0.7      | 0.3    |
| 62  | Full-time             | 13.5 | 6.6   | 1.2     | 0.9      | 1.3    |
| 81  | Part-time             | 17.6 | 3.4   | 2.0     | 0.8      | 0.8    |
| 82  | Full-time             | 13.1 | 5.9   | 2.2     | 0.1      | 2.4    |
| 101 | Part-time             | 17.2 | 3.1   | 2.3     | 0.5      | 0.8    |
| 102 | Full-time             | 14.9 | 6.3   | 0.7     | 0.6      | 1.9    |
|     | Group mean (SD) for 170 person-days | 16.8 | 3.2   | 2.0     | 0.5      | 1.3    |

Values in parentheses are 95% confidence limits.
After collecting questionnaire data it may be appropriate to conduct a set of experiments to measure the intensity and duration of exposure to the more toxic contaminants (not necessarily associated with the same effect) within one or more media (e.g., air, water, soil, food). A next logical step can be as simple as recommending personal or administrative approaches, and engineering solutions to mitigate exposure. Measurements to actually quantify any reduction in exposure can include microenvironmental, personal monitoring or biological markers techniques.

**Volatile Organic Compounds: An Example**

Exposure analysis for volatile organic compounds (VOCs) illustrates the general nature of direct and indirect methods needed to solve a problem. Based upon recent experience sources of VOCs are associated with a number of routes of exposure or specific microenvironments. These may lead to contact and exposures with high concentrations over a biologically relevant sampling interval (31–33). General environmental, micro-environmental or personal monitors can be employed during different phases of a study. However, difficulties arise because the requirements for sampling and analysis of VOCs can vary. Sorbent cartridge for personal monitoring vs evacuated canister for ambient monitoring (34). In addition, other variables must be considered. These are dependent upon the fundamental physical and chemical characteristics of the material, e.g., volatile versus semivolatile, and the types of activities and locations where human contact are anticipated to occur. For instance, the time of sampling is usually directly attributable to the analytical methodology available to detect the contaminants as well as the length of time a person might spend in a particular microenvironment, such as an automobile (35,36). Sampling time constraints can exist which may limit the type of sampling and analysis procedures available to attain the precise and accurate data for a particular set of VOCs.

Currently, major improvements in sampling and analysis are required to increase the number of chemicals detected by both microenvironmental and personal monitors. The limitations imposed by sampling in a confined space such as a room or by having a monitor attached to a person’s body present significant problems for detecting trace quantities of toxic pollutants (both organics and trace elements). As part of a workshop on gasoline exposures (34), the types of techniques available to measure the VOC constituents of gasoline for exposure analysis were reviewed. As seen in Table 6, sorbents and canisters are useful for a variety of projects. For instance, the technology is well developed for sorbent systems in personal monitoring studies. Both techniques have time resolution problems and other limitations that must be resolved to improve the measurements for exposure analysis.

Techniques available for personal monitoring of VOCs when coupled with exhaled human breath analysis, can provide data to relate the external exposure to the internal dose of the chemical and possibly the levels of a VOC or metabolite/adduct present in blood samples (37). The unique point here is that data can be collected as a chemical progresses from an external boundary (mouth or nose) to the lung (exhaled breath, and finally the quantity absorbed in the blood). Recent work in our laboratory has analyzed a specific case—chloroform—and the results from experimental studies have been used to validate the pharmacokinetics of chloroform disappearance in the exhaled breath over time. The work of Weisel et al. (38), shown in Figure 6, indicates that an individual exposed to chloroform during swimming, the chloroform in breath is associated with two processes: inhalation and dermal absorption of the chemical. The rate of removal for each route is dependent upon the route specific variables of uptake, transport, etc. This concept must now be generalized for more substances and complex systems that result in human exposure metabolism within the body (39).

Major challenges in designing studies of exposure–dose transformation or elimination are associated with establishing the detection limits for personal monitors (defines minimum sampling volume) and the half-time of elimination or transformation of the chemical from the blood (7,19,37). A wide range of concentrations may be present across a particular set of microenvironments, requiring a stringent set of criteria for selecting the type of sampling and analytical tools needed to establish exposure–dose relationships.

**Hazardous Waste Measurements: An Example**

The design used by Lioy et al. (21) for chromium is valuable for conducting exposure analyses at hazardous waste sites. Usually a hazardous waste site contains multiple chemicals, and the nature of the emissions are not definable by traditional emission tests. In fact, the emissions can be intermittent and change over the life cycle of a waste site.

At a waste site where there is an affected population or at least a population with suspected high exposures, it is first necessary to identify the primary media (soil, air, water, food) containing the contaminant and routes of entry to the body (9,12). In some cases human exposure involves passive contact such as inhalation or ingestion of a compound after it migrates through groundwater to potable water supplies or beneath the basement of a home. In contrast, human exposure can also be derived from active contact which includes riding a bike or playing on contaminated soil that contains respirable dust and the consumption of fish and seafood caught by local recreational fishermen (21).

External marker data required to reduce the uncertainty in a hazardous waste site risk assessment is normally beyond that required to complete a typical remedial investigation (RI), which has the primary purpose of defining the horizontal and vertical locations and movement of contamination on the site. A human exposure study would link the environmental measurements to a hazardous waste site risk or health assessment. A fundamental feature of a waste site investigation which accentuates the utility of external markers of exposure is the fact that many contaminants, such as benzene, and trichloroethylene, found at such locations are similar to materials encountered during daily life. Efforts must be made to define the microenvironments and the activity in the area surrounding a waste site which contribute to total exposure of one or more contaminants (12). Information from other studies could be used to provide baseline data on the incremental contribution from other sources. This will lead to greater success in identifying the magnitude of the exposures due to waste sites and the potential for high exposures. In the case of benzene, exposed individuals can be characterized with regard to sources of exposure based upon population exposure data, similar to that published by Wallace and found in Figure 7. The magnitude of the waste site contributions can be estimated for the out-
Table 6. Gasoline measurement methods matrix.

| Sample collection | Canister | Bags | Cryosorption |
|-------------------|----------|------|--------------|
| Charcoal          | (Summa polished) | Tedlar | Cryogenic trap |
| Tenax             | Teflon   |      |              |
| Carbosieve        | Mylar    |      |              |
| Sphercarb         |          |      |              |
| XAD-2             |          |      |              |
| Silica gel alumina (water protected) |          |      |              |

| Sample preparation | Method | Sample size | Point measurement | Batch variability | Capacity | Clean up | Very volatile gases and vapors | Reactive gas artifacts | Active sampler | Subject cooperation |
|--------------------|--------|-------------|--------------------|------------------|----------|---------|---------------------------------|----------------------|---------------|---------------------|
| Thermal desorption | Humidity adjustment | Time resolution | Time resolution | Time resolution | Time resolution | Time resolution | Time resolution | Time resolution | Time resolution |
| Solvent desorption | Pressurization | Sample size | Point measurement | Cost | Clean up | Pump contamination | Portability-personal | Reactive artifacts | Sample stability | Sample stability |
| Supercritical fluid desorption | Thermal treatment | Cost | Electrostatic effects | Active sampler | Portability-personal | Sample stability |
| Cryosorption       | Aliquot | Clean up | Electrostatis effects | Active sampler | Portability-personal | Sample stability |
| Oxidation (VOC CO2) | Cryofocus | Pump contamination | Active sampler | Solvent extraction | Solvent extraction | Solvent extraction |

| Analytical finish | Method | Limitations |
|-------------------|--------|-------------|
| Personal exposure | Source emissions | Time resolution |
| Indoor air        | Indoor air | Time resolution |
| Ambient air       | Ambient air | Time resolution |
| Standards compliance | Standards compliance | Time resolution |
| Headspace analysis | Headspace analysis | Time resolution |
| Vapor PM state    | Model development | Time resolution |
| Model development | Model development | Time resolution |

| Limitations | Method | Limitations |
|-------------|--------|-------------|
| Time resolution | Time resolution | Time resolution |
| Sample stability | Sample stability | Time resolution |
| Point measurement | Clean up | Time resolution |
| Batch variability | Cost | Time resolution |
| Capacity | Pump contamination | Time resolution |
| Clean up | Portability-personal | Time resolution |
| Very volatile gases and vapors | Pump contamination | Time resolution |
| Reactive gas artifacts | Reactive artifacts | Time resolution |
| Active sampler | Sample stability | Time resolution |
| Subject cooperation | Sample stability | Time resolution |

| Sample collection | Method | Limitations |
|-------------------|--------|-------------|
| Whole air         | Impinger | Cost |
| Whole air         | Charcoal | Sensitivity |
| Sorbant           | XAD     | Data interpretation |
|                   | PUF     | Data storage |

| Sample preparation | Method | Limitations |
|--------------------|--------|-------------|
| None               | Solvent desorption | Sensitivity |
|                   | Solvent extraction | Data interpretation |
|                   | Solvent extraction | Data storage |
|                   | Solvent extraction | Calibration |

| Analytical finish | Method | Limitations |
|-------------------|--------|-------------|
| GC-PID            | HPLC-UV | Source emissions |
| FID               | GC-FID | Source emissions |
|                   | GC-MS  | Source emissions |
| NDIR              | GC-Cyro/FTIR | Source emissions |
| LIDAR             | GC-MS  | Source emissions |
| FTIR              | HPLC-UV/Fluorescence | Source emissions |
| Pi-MS             | UV     | Source emissions |

| Applications | Method | Limitations |
|--------------|--------|-------------|
| Source emissions | Personal exposure | Time resolution |
| Indoor air    | Indoor air | Time resolution |
| Ambient air   | Ambient air | Time resolution |
| Standards compliance | Standards compliance | Time resolution |
| Model development | Time resolution | Time resolution |
|                 |                   | Time resolution |
|                 |                   | Time resolution |
|                 |                   | Time resolution |
|                 |                   | Time resolution |

| Limitations | Method | Limitations |
|-------------|--------|-------------|
| Cost        | Reactive gas artifacts | Time resolution |
| Sensitivity | Clean up | Time resolution |
| Data interpretation | Storage | Time resolution |
| Data storage | Batch variability | Time resolution |
| Calibration | Time resolution | Time resolution |
|             | Point measurement | Time resolution |
|             | Subject cooperation | Time resolution |

Abbreviations: MS, mass spectrometer; GC, gas chromatograph; FID, flame ionization detector; PID, photo ionization detector; FTIR, Fourier transform infrared; UV, ultraviolet; HPLC, high pressure liquid chromatography; XAD, a granular sorbent; PUF, polyurethane foam; Cyro, cryogenic; NDIR, non-dispersive infrared; LIDAR, laser radar.
door and indoor air for their residence or in their local community environment (40). If the results are equivocal, there may be a need to complete studies that quantify the contributions from other sources.

The magnitude of the data needed to properly characterize exposure at waste sites is difficult to imagine. A recent NRC report focused its evaluation on the more than 900 National Priority List sites. However, there are at least 3700 Department of Energy sites, and countless industrial and Department of Defense sites distributed across the United States (12). It is important to set priorities for the clean up, but agencies must not just rely on the number and amount of hazardous chemicals present at a site. This information must be coupled with population exposure data to account for the proximity and duration of contact in single or multiple media (41). In addition, the routes of exposure likely to occur for the gaseous or particle laden contaminants distributed across and within an unremediated area.

From the standpoint of public health, local populations with high exposures are a primary target, as well as large populations that have the potential for groundwater or reservoir contamination. Obviously, these two different situations require focused exposure characterization studies. For the former, both external and biological markers of exposure could be employed. The latter example may not require biological marker information. Both situations, however, would require microenvironmental measurements, and source–activity pattern questionnaires.

Models that can estimate the potential intensity of exposure must be designed to include site specific information and boundary conditions. This will assist in decreasing the uncertainty of any estimates. Clearly, models are necessary to define the mean exposures, but high exposure situations cannot be accurately predicted with generic (mean values or default factors) data (42,43). For such conditions the activities leading to high exposure would usually be site specific which precludes making accurate model estimates prior to a field investigation. Therefore, models and measurements must be applied iteratively during the exposure characterization of hazardous waste sites. This will improve the information on the distribution of exposure and also provide a firm foundation for dose estimates in a health assessment or an epidemiological study.

Conclusions

The field of exposure analysis has developed to the point where there is a “Tool Box” of external and internal markers available to test hypotheses on exposure-response relationships.

External markers of exposure can be selected that examine a person’s actual contact with a contaminant (Personal Monitors) or estimate population exposure from general environmental measurements.

External markers and internal markers of exposure do not a priori provide the investigator with the same type of information. Some studies may require both types of markers (exposure-reduction) while others may require the selection of one (risk assessment or epidemiology).

Exposure and pharmacokinetic models should be linked in order to understand the fundamental characteristics of human contact with a chemical and biologically effective dose.

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