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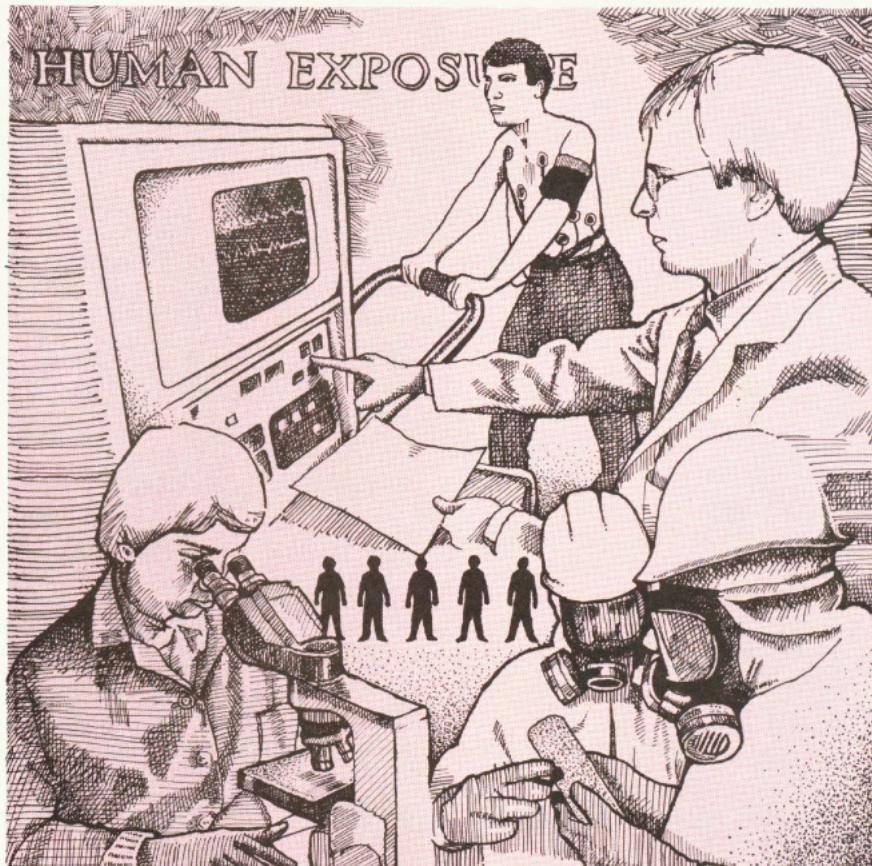
A multidisciplinary approach

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History has recorded numerous instances of human exposure to toxic agents in occupational and community settings. Notable examples are the London "Fumifugium" (sulfurous smog) of the 1600s; the British cholera epidemic in the 1840s, associated with the contamination of drinking water by sewage; the 20th-century air pollution episodes in London and Donora Valley, PA; black lung disease from mining coal; the catastrophic methyl diisocyanate explosion in Bhopal, India; occupational asbestos-related disease in the third quarter of the 20th century; and "Legionnaires" disease. In addition, each of us probably can describe anecdotal experiences of exposure to biological and chemical agents. The most common are occupational incidents which could have resulted in either acute or chronic health effects.

The systematic analysis of occupational exposure and health response began in this century as a result of the pioneering work by Alice Hamilton and others (1). Because an industrial environment usually has distinct boundaries, the potential sources of exposure to single and multiple chemicals are identifiable. The toxicity of the contaminants, however, and the routes and intensity of exposure that cause an effect have to be established. During the late 1930s various organizations began to accumulate information on the toxicity, exposure, and human health effects of contaminants. This led to the publication of the first set of workplace exposure limits (2); since then, the concept of exposure limits has been accepted by the industrial hygiene community.

Currently, threshold limit values



(TLVs) are available from the American Conference of Governmental Industrial Hygienists (ACGIH) for more than 600 chemicals (3), as are personal exposure limits (PEL), the federal standards promulgated by the Occupational Safety and Health Administration (OSHA), which were reauthorized in 1989 (4). Other federal agencies, such as the Food and Drug Administration, have implicitly set exposure limits by lowering the allowable content of toxic compounds and biological agents in foods, consumer products, and drinking water.

Until recently, community air pollu-

tion exposure for individual contaminants was estimated only from stationary monitors located outdoors or from emissions measured as they exit from a stack or process (5). Health-related ambient air standards still are based on these rudimentary concepts. The measurement strategies for exposure assessment, at least, have started to change as more information becomes available from personal monitoring, indoor air measurements, and outdoor activity related air monitoring (6-8). Some of the technical issues involved have been discussed in previous issues of *Environmental Science & Technology* (8-10).

and in work by Wallace and Ott (11) and Smith (12).

In 1986 and 1988, EPA drafted or published exposure assessment guidelines in conjunction with environmental risk assessment guidelines (13, 14). These provide general information on the factors that must be considered when single-medium and multimedia field or modeling studies are designed.

The purpose of this article is to identify current concepts that are used to evaluate human exposure to chemical and physical agents, areas in which various disciplines overlap, and future opportunities for research.

Exposure analysis and assessment

The concept of exposure analysis and its assessment is not new. Obtaining quantitative measures of exposure, however, and establishing their relationship to a biological effect are more complicated tasks. During the past 10–15 years, scientists and engineers with different backgrounds have conducted exposure assessments, and many situations require a multidisciplinary team to address the technical and scientific problems accurately. The types of experts and the information and disciplines that they may use for a given assessment are shown in Table 1.

The scientific features of a study must begin with the identification of the contaminant and its biological effects. The contaminant's movement and accumulation in the environment are described by established and new techniques for the measurement and modeling of various environmental media, including air, water, and soil. Toxicologists, epidemiologists, physicians, and other professionals provide the basic mechanistic and health effects information required to plan studies and define exposure-response relationships. The important task is to link these established approaches through the measurement and modeling of personal and population exposure by using the expertise that comes from one or more of the disciplines described in Table 1.

Through multidisciplinary approaches, the science of exposure is evolving into a coherent quantitative discipline that gathers information from environmental, toxicological, and health studies as well as from its own basic and applied experiments. A scientist working in this field eventually may be called an exposure analyst. The integration of physical, chemical, and biological information from various sources and the investigation of basic science issues related to human contact with contaminants would be part of his or her research activities. Further, as new strategies and tools become available, more effective

TABLE 1
Types of experts and areas of expertise required to conduct exposure research

Type of expert	Areas of expertise
Environmental scientist	Identification of contaminants, emissions, characterization of single-medium and multimedia physical and chemical processes, measurements
Engineer	Definition of process parameters, mass-balance on formation and release, controls, characterization, and instrumentation
Toxicologist and molecular biologist	Identification of biological endpoints, development of biological markers
Modeler (various major disciplines)	Environmental emissions, transport, and fate; chemical kinetics; physiologically based pharmacokinetics and dynamics; individual and population exposure (time-activity); risk assessment
Social scientist	Questionnaire development, population behavior and activities, habits
Statistician	Study design, power calculations, data analysis
Epidemiologist	Collaboration on identification of human exposure-biological response relationships
Physician	Identification of worst case situations, population selection, exposure-response studies
Industrial hygienist	Identification of contaminants and persons most at risk, time-activity profiles in workplace

laboratory and field studies of single and multiple exposure routes can be planned. Results from these studies will impel government and industry to take appropriate exposure reduction measures for individuals or for the general population.

The concept of a continuum from the source of a pollutant to its proximate or ultimate effect (Figure 1) is a basic feature of any exposure-dose-effect investigation based on a single route (15). In the case of total exposure this continuum can include multiple routes. Each route may additively or synergistically contribute to an exposure-dose-response relationship. The dose derived from contact with each medium is the usual means by which significant human exposures are compared (12, 16, 17).

The tasks that require applications of quantitative exposure studies include risk assessment, environmental epidemiology, risk management, clinical diagnosis, and prevention of disease. Before any attempt to apply exposure assessment to each, it should be noted that the most important route of exposure may not always be easily ascertained. This is a crucial point, because immediately reducing analytical procedures to deal with a single route of exposure may not be scientifically sound. It is more logical to consider a person's potential contact with all media and to reduce or increase the level of concern for a route of exposure entry to the body after a review of available data and of preliminary measurements. Exposure studies can be designed to identify a specific

population at risk, define norms for the general population, or examine long-term effects of the reduction or increase of exposure to a contaminant by monitoring selected groups or the general population.

Total exposure and dose

A person's exposure to a contaminant in the community environment and/or workplace is defined as "the contact at one or more boundaries (e.g., mouth and skin) between a human and a contaminant(s) at a specific concentration(s) for a period of time." Total exposure consists of increments from all media (soil, water, food, air, plants) that contain a contaminant and all routes of entry (inhalation, ingestion, dermal).

Mathematically, exposure is defined as:

$$E = \int_{t_1}^{t_2} C(t) dt \quad (1)$$

where E is exposure; $C(t)$ is a concentration, which varies as a function of time; and dt is an increment of time from t_1 to t_2 .

Researchers have attempted to examine total exposure of an individual to a single contaminant, but in most cases their studies have been based on a subcategory of the available pathways or have been conducted for a limited period of time (10, 18–21). For total exposure, data should be gathered for all significant media and routes of entry

from microenvironmental and personal measurements and from modeling studies. These data can be used to estimate the intensity and duration of exposure and to assess its relationship with known health effects.

The weakest links in exposure studies usually are associated with disciplines that are not adequately represented during the design phase of the study. Also, as stated by Stevens and Swackhamer (22), some exposures are estimated from weak data bases and from data with large uncertainty, or are inferred from measurements made for purposes other than assessing exposure. Therefore, a carefully designed study should acquire information on the plausibility of measuring or estimating exposure, obtaining reliable data on contact with a contaminant in one or more media, and attributing a specific biological effect to exposure. This approach basically integrates and expands strategies presently employed for one medium, but provides more realistic information on the incremental features of exposure to a contaminant.

The EPA exposure guidelines for risk assessment actually define exposure as a *potential dose*, because the units are those of mass (e.g., $\mu\text{g}/\text{kg}/\text{day}$ or $\text{mg}/\text{kg}/\text{day}$) (14). However, the amount deposited on or absorbed by an organ interface is not estimated, but is implicitly assumed to be 100%. This is a significant departure from traditional approaches to identifying exposure. Suppose the guidelines restate the definition as a potential dose and reformulate to the following equation:

$$D_p = \int_{t_2}^{t_1} C(t)f(x)dt ; f(x) = CR \quad (2)$$

where D_p (mass or mass/body weight) is potential dose; $f(x) = CR$, the contact rate (e.g., m^3/time , for inhalation; mass/time for ingestion; area/time for dermal exposure); and the contaminant is assumed to be 100% absorbed or adsorbed. The guidelines, then, would be consistent with the definitions of exposure and dose. In general, EPA guidelines for exposure measurement have the correct approach because ultimately, the only effective way to compare multimedia contributions of a contaminant is through the values determined for a potential (14), internal (23), or biologically effective dose (23).

As depicted in Figure 1, quantitative exposure values can be used in various estimates of dose from each medium. The dose can be represented by the general equation:

$$D = \int_0^t D(t)dt = \int_0^t f(x)g(ab)p(as,rd,me,el) C(t)dt \quad (3)$$

where D is an integrated dose (mass or mass/body weight) at a target tissue or cell; $D(t)$ is a time-varying function for

dose; $f(x)$ is the contact rate; $g(ab)$ is a variable dependent on the target organ or system, and the bioavailability that affects the extent of absorption (ab); and $p(as,re,md,el)$ is a variable dependent on the nature of a contaminant's assimilation (as), the cell repair or damage (rd), elimination (el), and metabolism (me).

The most appropriate forms for expressing dose would be the internal or biologically effective dose, but one can use the potential dose by assuming a 100% absorption. All can be calculated from Equation 3 with certain assumptions.

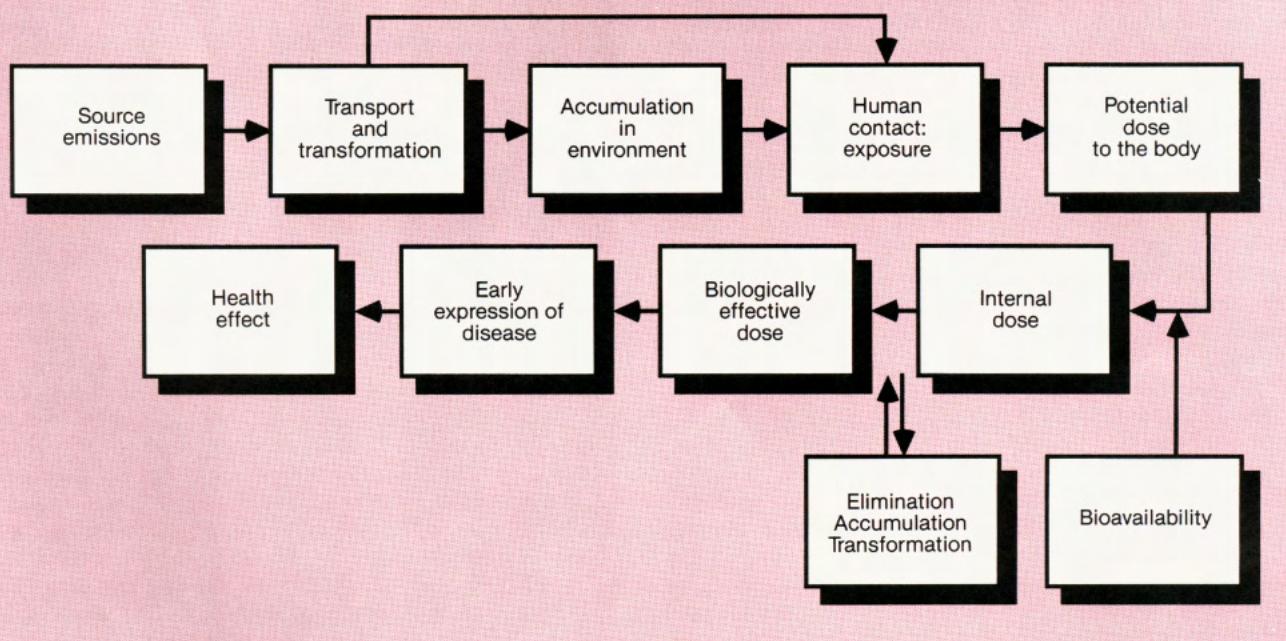
For the *potential dose*, described in Equation 2, $g = 1$, $p = 1$; and $f(x)$, a contact rate, is estimated for each route of entry in units of volume surface or mass per unit time. The potential dose can be used to estimate the mass of a contaminant just prior to deposition on, or passage through, a membrane or, as stated above, which is 100% absorbed. The form of the equation would be:

$$\int D_p(t)dt = \int f(x)C(t)dt \quad (4)$$

The units of D_p are in μg or $\mu\text{g}/\text{kg}$.

For the *internal dose*, $p = 1$, and the rate of absorption or adsorption defines g . Actual values of internal dose can be estimated from measurements of the contaminant; metabolites; or other derivatives in cells, tissues, or fluids (15). Examples of indicators that can be used to derive an internal dose are volatile organics in breath, trace elements in blood,

FIGURE 1
Continuum from emission of a contaminant to a health effect



and numerous compounds and metabolites in urine. To calculate an internal dose, the variables used for $g(ab)$ require values for the deposition in the lung, absorption through the epidermal layers of the skin, or other routes of exposure. The form of the equation would be:

$$\int D_1(t)dt = \int f(x)g(ab)C(t)dt \quad (5)$$

The *biologically effective dose* is associated with a fraction of a material at a site of action and is calculated by estimating values for p (23). It is used to calculate the amount of a contaminant (or metabolite) that interacts with cellular macromolecules at a site and results in altered physiologic function. The form of the equation for $D(t)$ would be identical to that of Equation 3.

Many types of chemical, physical, and biological information must be used for comparing doses from different media (see box below) (24, 25). It is apparent that all of these factors cannot be measured directly in an individual or in the general population. Through multidisciplinary efforts, however, the parameters with the highest degree of uncertainty can be identified and new experiments planned to provide adequate data for constructing models. Each situation may need measurements of the concentration(s) of the contaminant(s); information available from questionnaires; and other basic research in the science of exposure, toxicology, and controlled human studies (18, 26, 27).

Linking exposure and effects

As exposure studies are used more frequently to examine complex multi-

media situations, data bases for many contaminants will expand for use in microenvironmental and personal exposure models (16, 18, 21, 22, 28). Exposures of individuals, subgroups, and the general population then can be estimated for one or more microenvironments and situations that require exposure reduction strategies. It is essential that modeling studies be able to focus on the extremes of a population distribution that are exposed to a specific contaminant, including the individual or subgroup that is subjected to the most exposure. These data would be used in conjunction with estimates of the mean "normal" exposure to the general population or a statistically representative subgroup in order to categorize the severity or intensity of exposures.

A recent review article by Stevens and Swackhamer indicated the need to link environmental source, transport, and receptor models to estimates of exposure (22). One of the major modeling research initiatives will involve the development of personal exposure models that include the individual as a compartment within algorithms that also describe the environmental transport and accumulation of contaminants. Stevens and Swackhamer also alluded to the need for incorporation of biological data (22). Therefore, another step to help characterize pollutants and conditions of concern and to decrease the uncertainty in the estimates of exposure will be the integration of environmental and exposure models mentioned above with toxicokinetic and pharmacodynamic models for acute and chronic effects (29).

The purpose of an exposure-dose-effect model would be to relate tissue concentrations and damage to the intensity of exposure and processes controlling absorption, reactions, and effects. Analyses of these models could provide quantitative information for each component of Figure 1. Examples of the types of information required for such models are identified (see box on next page). Ultimately, the models can be used to estimate a mass balance between the mass prescribed to the individual for various sources, the amount internalized, and the amount available to target sites (cells and organs). Cellular transformation and repair data would be derived from toxicological studies. The human dose would be estimated from exposure and epidemiological studies of all pertinent routes of exposure.

Also, it should be recognized that a particular chemical or agent available for inhalation, ingestion, or dermal absorption may affect more than one specific target tissue and cause one or more health effects. Therefore, the concentrations of the contaminant and its transformed metabolites and adducts should be estimated at one or more target sites (15).

Measurement of exposure

The measurement of exposure has advanced more quickly than the strategies required to assess exposure. Three general types of measurement are direct (personal), indirect (microenvironmental and questionnaires), and biological monitoring. Articles by Ott (9, 30), Spengler (8), Wallace (3), and Smith (12) have dealt with the issues of personal and microenvironmental monitors for the inhalation route. Multimedia monitoring has been discussed by Severn (10), Stevens and Swackhamer (22), and Lippmann and Thurston (31).

A detailed example: Inhalation. The recent major advances in measuring inhalation exposure within community environments illustrate how the measurement and estimation of exposure have been redirected from considering only area measurements to including microenvironmental and personal measurements. This redirection appears somewhat contradictory, because industrial hygienists have employed personal air monitoring techniques successfully for years (32). It must be remembered, however, that in most occupational situations, excluding tight office buildings, the concentrations of a contaminant are orders of magnitude higher than those present in the community or outdoor environment. Consequently, the detection limits, sensitivity, and precision and accuracy requirements are more severe

Exposure-dose-response modeling studies

- I. Parameters needed to identify exposure and internal dose
 - A. Route of entry, concentrations, intensity
 - 1. Air
 - 2. Water
 - 3. Soil
 - 4. Food
 - B. Contact rate and frequency
 - 1. Inhalation
 - 2. Skin deposition
 - 3. Ingestion
 - C. Internal partitioning
 - 1. Deposition in lungs and absorption
 - 2. Skin absorption
 - 3. Gastrointestinal absorption
 - 4. Elimination
- II. Definition of the compartments to be modeled
 - A. Identification of toxic contaminants and realistic human contact
- B. Animal studies
 - 1. Dose (mass or mass/kg of body weight)
 - 2. Lowered high dose rate (mass/time) including low to high dose extrapolations
 - 3. Tissue response
 - 4. Reversible and nonreversible effects
- III. Parameters of concern in compartments
 - A. Diffusion to target sites
 - B. Body circulation of contaminants
 - C. Reaction and/or metabolism
 - D. Storage in tissues
 - E. Elimination (half-life in tissues)
 - F. Fluid-surface partitioning
 - G. Surface-tissue partitioning
 - H. Tissue damage (repair and effect rates)

for the community setting (3, 8, 33).

The traditional method for community air sampling has been to place continuous samplers, usually for gases, and integrating samplers, usually for particles, at one or more fixed sites in a city or rural area (5, 29). These provide information on contaminant concentrations in outdoor air and have been used to estimate an individual's average acute or lifetime exposure (12, 26). It is assumed that all contact with the pollutant would be represented by the outdoor concentrations measured by a stationary monitor. Because of the high

concentrations of SO₂, total suspended particulates (TSP), CO, and other compounds present in the ambient atmosphere in the United States until the 1970s, this may have been a valid assumption (34) that still may be valid in many less developed countries.

Emission controls placed on major outdoor sources in the United States during the last 20 years have significantly reduced the concentrations of the above pollutants. On the other hand, people are more concerned about emissions of many pollutants by indoor sources because they know buildings

were made more airtight during the energy crisis, synthetic materials for furniture and furnishings were introduced during the 1970s, humans spend 80–90% of their time indoors, and higher indoor concentrations of certain contaminants have been measured (6).

Outdoors, however, ozone remains a problem pollutant. It often exceeds the National Ambient Air Quality Standards (NAAQS), persists over large areas, and has few major indoor sources (35). Therefore, an outdoor site still can be used to estimate the primary microenvironments of high exposure with-

Parameters required to calculate the potential and internal dose

Airborne contaminant

- I. Concentrations ($\mu\text{g}/\text{m}^3$, ppb)
 - A. Microenvironments
 - B. Personal
- II. Patterns of exposure
 - A. Intensity "episode" concentrations versus normal levels (average)
 - B. Frequency and duration of contact
- III. Transport
 - A. Dispersion and advection
 - B. Other meteorology related to removal rates (washout, fallout)
 - C. Indoor ventilation and removal rates
- IV. Chemistry
 - A. Formation rates
 - B. Transformation rates
- V. Deposition rate ($\mu\text{g}/\text{cm}^2$)
 - A. Environmental
 - B. Lung
- VI. Contact
 - A. Inhalation (dependent on exercise regime) (m^3/time)
 - B. Dermal deposition and permeability ($\mu\text{g}/\text{cm}^2/\text{time}$)
 - C. Ingestion (food, soil) ($\mu\text{g}/\text{g}/\text{time}$)
- VII. Absorption
 - A. Within tissue
 - B. Into the blood and other fluids

Water contaminant

- I. Concentration ($\mu\text{g}/\text{L}$, ppm)
 - A. Tap water
 - B. Water uses
 - C. Effluent
 - 1. Industrial
 - 2. Commercial
 - 3. Residential
 - 4. Uncontrolled dumps
- II. Patterns of exposure
 - A. Drinking
 - B. Swimming
 - C. Cooking
 - D. Bathing
 - E. Laundry
 - F. Showering
- III. Solubility of contaminant

IV. Volatility of contaminant

- V. Transport
 - A. Groundwater
 - B. Surface water
 - C. Domestic supply
- VI. Chemistry
 - A. Formation rates
 - B. Transformation rates
 - C. Degradation
- VII. Contact rate ($\mu\text{g}/\text{L}/\text{time}$) via exposure route
 - A. Ingestion
 - B. Skin
 - C. Inhalation (volatilized)
- VIII. Absorption
 - A. Dermal deposition and permeability
 - B. Gastrointestinal tract

Soil and sediment

- I. Concentrations ($\mu\text{g}/\text{g}$)
 - A. Dusts
 - 1. Outdoor
 - 2. Indoor
 - B. Contaminated soil
 - 1. Uncontrolled dumps
 - 2. Airborne deposition
 - 3. Landfills
 - 4. Resuspension
- II. Patterns of exposure
 - A. Frequency and duration
 - B. Intensity of contact
- III. Percolation rate
 - A. Soil composition
 - B. Water table
 - C. Solubility
 - D. Transport
- IV. Volatilization
 - A. Contaminant
 - B. Soil composition
 - C. Top soil and cover
- V. Contact rate via exposure route
 - A. Dermal deposition and permeability
 - B. Lung
 - C. Gastrointestinal tract (pica)
 - 1. Normal population
 - 2. Abnormal ingestion behavior

VI. Body parameter

- A. Lung volume
 - B. Exposed skin surface (condition of skin)
- VII. Absorption
 - A. Soil composition
 - B. Contact and absorption rates

All media: Can be supplemented by measuring a biological marker of accumulated single-medium or multimedia exposures in blood, urine, feces, and so forth. Many of these usually are nonmedia specific.

Body weight: Used for lifetime exposure and dose calculation.

Food (commercial and homegrown produce)

- I. Concentrations ($\mu\text{g}/\text{g}$)
 - A. Plants
 - B. Vegetables and fruit
 - C. Milk
 - D. Animals and fish
 - E. Cooked foods
 - F. Beverages and water-based foods ($\mu\text{g}/\text{L}$)
- II. Patterns of exposure
 - A. Rate ($\mu\text{g}/\text{L}/\text{time}$) ($\mu\text{g}/\text{g}/\text{time}$)
 - B. Frequency
 - C. Origin of food
 - 1. Home grown
 - 2. Commercial distribution
 - 3. Local farms
 - 4. Processed foods
- III. Source of contamination
 - A. Naturally occurring contaminants
 - B. Airborne deposition
 - C. Fertilization
 - D. Pest control
 - E. Waste dumps
 - F. Water supply
 - G. Preparation and cooking techniques
- IV. Contact rate
 - A. Gastrointestinal (GI)
 - B. Inhalation (cooking only)
- V. Absorption through GI tract

in the general population, because people have been shown to suffer acute health effects from being exposed to ozone for 1–8 h for specific concentration ranges (36).

By contrast, as clearly shown in the Total Exposure Assessment Methodology (TEAM) studies (7, 37–40), for a statistically selected subgroup of the population, a person's exposure to individual volatile organic compounds (VOCs) can be associated with indoor rather than, or in addition to, outdoor sources. This makes a single outdoor site inadequate for identifying all of the opportunities for reducing general population exposure to VOCs. Currently, the significance of long-term low exposures or subchronic exposures to VOC in causing biological effects needs to be verified by epidemiological studies and, when possible, by toxicological studies that use dose ranges near realistic levels and appropriate durations of exposure.

Developments in the technology for the microenvironmental monitoring of indoor air have defined new ways people are exposed to contaminants and have established means for conducting personal monitoring. One approach to a study of the inhalation route should account for person-contaminant contact in particular locations by adding contaminant contributions over time, as measured from microenvironmental samples taken at indoor and outdoor sites, and during transportation or commuting. This is characterized as the *indirect* exposure approach. The alternative approach calls for complete personal sampling while information is gathered on the potential active and passive contact between the person and the contaminant; this is known as the

direct exposure approach. In either case, the sampling frequency, time interval, and concentration patterns should be linked to the time of biological response of the body to a specific contaminant.

Personal measurement techniques are beginning to appear in applied studies (8, 11, 41–45). The detection limits and reliability of personal samplers need to be improved. In addition, research on personal activity questionnaires and on automated personal location monitors is necessary, because such instruments are extremely valuable in defining the personal activities that result in active and passive exposure.

Other media and routes of exposure. Techniques for the measurement and assessment of exposure to contaminants in media other than air also require development. Specific protocols for drinking-water sampling have been used for years, and the usual approach to exposures analysis has been to assume a person drinks 2 L/day of tap water. The range of consumption for all fluids, however, can be below this value (46).

On the basis of the contaminant measurement requirements of the Clean Water Act, the number of compounds routinely measured in drinking water, surface water, and groundwater has increased to well over 100 (47, 48). However, systematic approaches are needed to examine the actual patterns of water consumption and other types of exposure to water (49, 50), such as swimming and showering. We need to determine whether the estimates of exposure from ingestion adequately account for the portion not derivable from dermal and inhalation contact (e.g., showering, swimming, bathing) and whether con-

centration measurements made for compliance or regulation are frequent enough to estimate exposure adequately. If not, what is a better approach to sampling?

Measurements of community exposure to contaminants that migrate from underground storage tanks and hazardous waste sites need to be conducted (5, 51). People are exposed when they drink groundwater from wells, but to date many assessments have used surrogate markers of exposure, such as the geographical location of a potentially exposed population. Studies should be conducted that couple groundwater infiltration with the possible volatilization of a compound in the home and with other forms of contact. In addition, contaminant concentration and mobility data are essential for validating groundwater transport and environmental fate models, and these must be integrated with exposure models to define populations at risk (28).

Dermal exposure studies have been conducted for a number of different classes of compounds, especially for farm workers exposed to pesticides. A fluorescent tracer technique has been developed for studies of workers that helps identify the points of contact of a contaminant with bare and covered skin more accurately (52). This technique now is being tested for use in the community environment; children indoors and outdoors are the principal subjects. The internal dose received from dermal exposure also needs to be quantified for compounds of environmental significance, such as pesticides and hazardous wastes. Their absorption is estimated from well-known factors, but compound-specific and matrix-specific differences can affect the amount of a compound absorbed by the skin (53). For instance, lead acetate normally is not readily absorbed by the skin, but if it is contained in an oil, it becomes extremely absorbable. Thus, we need research on the amount of a compound deposited, how it remains on or is absorbed through the skin, and its rate of absorption.

Soil ingestion and inhalation have been investigated in a number of exposure assessment studies (10, 19, 20, 53, 54). Standard methods are available for sampling the surface of a site and for taking core samples (55). Estimates have been made of the quantity of soil ingested by children and adults, and ingestion rates range from mg/kg to g/kg per day (46). The amount retained in the body can be estimated by using the gastrointestinal absorption rates for contaminants (20). A recent exposure assessment, however, has indicated that a gastrointestinal absorption of 30% for

Setting priorities for health outcomes

Integrated models for assessing exposure and dose appear to require seven basic steps to set priorities for the health outcomes from doses received by cellular tissue. As modified from the work of Smith (30) these are:

- Identification of agents, media and routes of exposure;
- Identification of target tissue and routes of entry;
- Identification of the uncertainty in each data base;
- Development of a toxicokinetic model for the agent and the target tissues;
- Development of a quantitative pharmacodynamic model of the effects caused by the agent in the target tissue;
- Design of a strategy to collect the appropriate exposure data;
- Application and validation of models to estimate tissue concentration and exposure index and analyze epidemiological data.

The first two steps define the problem, the third and fourth steps provide the theoretical framework to formulate the models, the fifth step reduces uncertainties in model variables by gathering new data, and the last step implements the model. For many contaminants these data are not currently available; thus it will be a challenging task to develop novel approaches for validating individual components and compartments of a total model.

tetrachlorodibenzo-*p*-dioxin (TCDD) is "most tenable" (56).

The measurement and estimation of exposure via soil dust need to be focused on particular locations at which a population may be exposed to reentrained soils. One must not assume, for instance, that a population will not be closer than 200 m from hazardous compounds contained in soils. Unfortunately, many dispersion models do not include near-field concentration patterns (57). In addition, once the dust is deposited in a home its resuspendability must be determined because the factors currently used to estimate indoor exposures to soils are based on little quantitative information (20). EPA is conducting soil ingestion studies (10). The agency's objective is to reduce the uncertainty in estimates of the amount of material ingested by a child or adult. These types of analyses must be linked to current and future exposure studies to ensure that potential sources and high-dose situations are not ignored. For example, in the case of pesticides, it is important to remember that a child could be in contact with a treated carpet for some time after the exterminator has left the house.

Another important medium of concern is food. Much information is available from food basket surveys on the average amounts of vegetables, meat, fish, beverages, and poultry consumed by the general population (58). This can be found in tabulations such as the EPA Exposure Factors Handbook (46). The difficulty is that food-basket surveys are generic, and even with the increased availability of contaminant data, they are inadequate for determining the exposure of a specific population to a specific contaminant.

A good example is the compound benzo[*a*]pyrene (BaP). It is found in vegetables and other foods (59). The amount of BaP present in cooked foods will vary, depending on the method of preparation. Therefore, to estimate a person's exposure to BaP one must know the origin, composition, and method of preparation of his or her diet to minimize overestimation or underestimation of exposure to BaP.

The Total Human Environmental Exposure Study (THEES) set up composites of the daily meals of each participant throughout each two-week period of study. An estimate of BaP consumption was obtained for comparison with measurements in all other media. The exposure of individuals varied greatly and depended on individual cooking and eating habits (44). The significance of *food* exposure versus *inhalation* exposure varied from individual to individual; individual internal inhalation dose

to food dose ratios ranged from 0.01 to 10. These observations indicate the need to examine each individual together with classes of compounds associated with food preparation, and suggest ways to develop more standardized approaches to developing composites of meals.

Further consideration must be given to the linking of biological markers of exposure, defined as a contaminant or metabolite that is measured in a compartment within the body, with direct and indirect measurements of exposure of one or more media. The most useful biological media are urine, blood, nails, hair, breath, and adipose tissue.

The National Academy of Sciences (NAS) has recently published reports on the types of markers available or being developed for pulmonary and reproductive effects (23, 60). These reports strongly recommend that these markers be used to identify exposed populations and to provide baseline values for these markers in humans. However, one major concern of the exposure analyst was not adequately expressed in the EPA guidelines or in the NAS reports: the need to take samples for direct and indirect measurements of contaminant exposure within similar or equal periods of time. Without such measurements, biological marker data are of limited usefulness in providing information on the segments of the continuum (Figure 1) to the left of "internal dose." Exceptions would be cases in which the contaminant exists almost exclusively in one medium and is derived from a single source or type of source (e.g., motor vehicles).

If direct and indirect measurements of exposure are integrated into a study design, biological markers will become important tools that indicate when a person has been exposed, why, and how. Alone, a biological marker of exposure can give quantitative information on a specific contaminant, but it will fail to identify the sources and the routes and duration of exposure.

Time-activity patterns

Incorporating biological measurements with time-activity patterns will reduce the number of assumptions made about where an individual's exposures occurred for a contaminant found in a medium or media. Establishing the activity patterns for an individual or a statistically selected portion of the population will increase our ability to identify the sources that contribute to an acute or chronic effect. For some pollutants, such as ethylene oxide, the sources and location of potential exposure are few, which helps pinpoint the exposure. In other cases, such as lead, the activities that cause an exposure will be much

more complex (31). For the air pollutant carbon monoxide, sophisticated time-activity models have been developed and measurements have been made in a number of different microenvironments, but models that define the sources and locations of exposure still are only partially validated (16, 42, 43).

Information on activities is being collected by means of questionnaires and, more recently, with personal activity data loggers worn by individuals. These data improve the accuracy of exposure measurements by providing better estimates of population activities and the time associated with each.

Regulatory aspects. The challenge in the future will be to incorporate exposure data in the development and analysis of the criteria for EPA's NAAQS and for standards used to minimize exposures to contaminants found in other media. A curious contrast to the approaches currently in use to set environmental standards for pollutants in a single medium is the exposure assessment guidelines for risk assessment developed by EPA (14). The latest, improved version provides general information on the scientific features that must be considered and completed before conducting an assessment to be used in the estimation of risk. These include summing the measurements and estimates of a contaminant for all microenvironments associated with one medium and setting priorities for the contributions from all media; this could be a major advance. Basic and applied research on exposure problems will result in more effective applications of total exposure assessment.

Future versions of the guidelines need to state specifically that measurements should be coupled to a relevant biological response time (18, 45). For example, a few measurements of a carcinogen in the ambient or indoor air or water are not adequate for establishing a basis for lifetime exposure. A person could be presented with many opportunities for exposure to a compound during one month and with many more during a lifetime. Therefore, the level of his or her exposure on a few days each year may not be truly representative.

The source-to-effect continuum

Understanding the continuum from source to effect requires a synthesis of ideas expressed by individuals with different backgrounds who conduct exposure analysis and assessment. It appears that exposure assessment has the potential to link (a) environmental measurements and model predictions for sources transport and fate with (b) the results of dose calculations made from toxicological data and environmental science

health effects studies. The continuation of recent research will improve the scientific basis required for conducting human exposure measurement and modeling studies, and for making judgments on what contaminants in what settings require exposure reduction strategies.

The above examples of the types of information required to develop a data base for completion of a total exposure study should be used to design coherent studies that can rank potential exposures of individuals or statistically selected sub-groups of the population to each medium. The medium-specific aspects of the measurement (sampling) and the estimation (modeling) of exposure also can be used to identify the important routes of entry to the body. As the analysis of exposure evolves and provides new and better data bases, it will identify the populations at risk and activities that lead to exposures and adverse health effects.

Acknowledgments

I wish to thank the members of the NAS Committee on Advances in Exposure Assessment to Airborne Contaminants, who have had significant influence on my concept of exposure assessment; Dr. K. Hulebak of ENVIRON for her comments and continued discussion on major issues; G. Akland of EPA for his review and comments on an earlier draft of this manuscript; and Dr. Clare Franklin of Health and Welfare Canada for her timely insights.

This article was reviewed for suitability as an ES&T feature by Joan Daisey, Lawrence Berkeley National Laboratory, Berkeley, CA 94720; and William C. Nelson, EPA, Research Triangle Park, NC 27711.

References

- (1) Alice Hamilton, *A Life in Letters*; Sicherman, B., Ed.; Harvard University Press: Cambridge, MA, 1984.
- (2) Corn, J. K. *Applied Ind. Hyg.* **1988**, 1(3), F8–F11.
- (3) *Threshold Limit Values and Biological Indices, 1988–89*; American Conference of Governmental Industrial Hygienists: Cincinnati, OH, 1988.
- (4) Code of Federal Regulations; 29 CFR 1910.1000, **1989**; OSHA 3112.
- (5) Lioy, P. J. In *Community Air Sampling Strategies, Air Sampling Instruments*, 7th ed.; S. Hering, Ed.; American Conference of Governmental Industrial Hygienists: Cincinnati, OH, 1989; Chapter D.
- (6) National Research Council Committee on Indoor Air Pollutants. *Indoor Air Pollutants*; National Academy Press: Washington, DC, 1981.
- (7) Wallace, L. A. *Total Exposure Assessment Methodology (TEAM) Study, Summary and Analysis*, Vol. 1; U.S. Environmental Protection Agency: Washington, DC, 1987.
- (8) Spengler, J. D.; Soczek, M. L. *Environ. Sci. Technol.* **1984**, 18, 268A–80A.
- (9) Ott, W. R. *Environ. Sci. Technol.* **1985**, 19, 880–86.
- (10) Severn, D. J. *Environ. Sci. Technol.* **1987**, 21, 1159–63.
- (11) Wallace, L. A.; Ott, W. R. *J. Air Pollut.* **1982**, 32, 601–10.
- (12) Smith, K. *Environment* **1986**, 30, 10–38.
- (13) *Fed. Regist.* **1986**, 51, 33992–34054.
- (14) *Fed. Regist.* **1988**, 53, 48830–53.
- (15) Committee on Biological Markers, National Research Council. *Environ. Health Perspect.* **1987**, 74, 3–9.
- (16) Ott, W. R. *J. Toxicol. Clin. Toxicol.* **1983–84**, 21, 97–128.
- (17) Ott, W. R. *Environ. Int.* **1982**, 7, 179–96.
- (18) Schmidke, N. W. In *Human Exposure Routes to Persistent Toxic Chemicals in the Great Lakes Basin: A Case Study*; Davies, K., Ed.; Lewis: Chelsea, MI, 1988; Chapter 10.
- (19) Travis, C. C.; Hattemer-Frey, H. A. *Chemosphere* **1987**, 16, 2331–42.
- (20) Hawley, J. K. *Risk Analysis* **1985**, 5, 289–302.
- (21) Sexton, K.; Ryan, P. B. *Assessment of Human Exposure to Air Pollution: Methods, Measurements and Models, Air Pollution, The Automobile and Public Health*; National Academy Press: Washington, DC, 1988.
- (22) Stevens, J. B.; Swackhamer, D. L. *Environ. Sci. Technol.* **1989**, 23, 1180–86.
- (23) National Research Council Subcommittee, Committee on Biologic Markers. *Biologic Markers in Reproductive Toxicology*; National Academy Press: Washington, DC, 1989; pp. 1–381.
- (24) Howard, P. H. In *Handbook of Environmental Fate and Exposure Data for Organic Chemicals*; Lewis: Chelsea, MI, 1989; pp. 1–574.
- (25) Agency for Toxic Substances and Disease Registry. *Health Assessment Format, Guidelines and Methodology*; Agency for Toxic Substances and Disease Registry: Atlanta, GA, 1989.
- (26) National Research Council Committee on Epidemiology of Air Pollution. *Epidemiology of Air Pollution*; National Academy Press: Washington, DC, 1985.
- (27) Total Human Exposure Research Council (THERC). *Research Needs in Human Exposure: A 5-Year Comprehensive Assessment (1990–1994)*; Office of Research and Development, U.S. Environmental Protection Agency: Washington, DC, 1988.
- (28) Nazaroff, W. W.; Cass, G. R. *Environ. Sci. Technol.* **1986**, 20, 924–34, 986.
- (29) Smith, T. *Am. J. Int. Med.* **1984**, 12, 249–68.
- (30) Ott, W. R. *J. Air Pollut. Control Assoc.* **1977**, 27, 543–47.
- (31) Lippmann, M.; Thurston, G. D. *Arch. Environ. Health* **1988**, 43, 113–23.
- (32) Ayers, H. In *Air Sampling Instruments*, 7th ed.; S. Hering, Ed.; American Conference of Governmental Industrial Hygienists: Cincinnati, 1989; Chapter C.
- (33) Samet, J.; Marbury, M. C.; Spengler, J. D. *Amer. Rev. Respir. Dis.* **1987**, 136, 1486–1508.
- (34) Eisenbud, M. *Bull. New York Acad. Med.* **1978**, 54, 991–1011.
- (35) “National Air Quality and Emissions Trends Report, 1987”; U.S. Environmental Protection Agency: Research Triangle Park, NC, 1989; EPA-450/4-89-001.
- (36) Lioy, P. J.; Dyba, J. *Toxicol. Ind. Health* **1989**, 5(3), 493–504.
- (37) Wallace, L. A. et al. *Atmos. Environ.* **1984**, 35, 293–319.
- (38) Wallace, L. A. et al. *Atmos. Environ.* **1985**, 19, 1651–61.
- (39) Wallace, L. A. et al. *Environ. Int.* **1988**, 12, 369–87.
- (40) Wallace, L. A. et al. *Atmos. Environ.* **1988**, 22, 2141–63.
- (41) Lewis, R. G.; Mulik, J. D. In *Advances in Air Sampling*; Lewis: Chelsea, MI, 1988; pp. 117–31.
- (42) Akland, G. G. et al. *Environ. Sci. Technol.* **1985**, 19, 911–18.
- (43) Ott, W. R. et al. *Atmos. Environ.* **1988**, 22, 2101–13.
- (44) Lioy, P. J. et al. *Arch. Environ. Health* **1988**, 43, 304–12.
- (45) Rappaport, S. M. In *Advances in Air Sampling*; Lewis: Chelsea, MI, 1988; pp. 337–52.
- (46) *Exposure Factors Handbook*; U.S. Environmental Protection Agency: Washington, DC, 1989; EPA-600/8-89-043.
- (47) *EPA Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water*; Environmental Monitoring Support Laboratory: U.S. Environmental Protection Agency: Cincinnati, OH, 1986.
- (48) *Drinking Water and Health*, Vol. 1; National Research Council: Washington, DC, 1977.
- (49) Andelman, J. B. *Environ. Health Perspect.* **1985**, 62, 313–18.
- (50) Wan-Kuen Jo. Ph.D. Thesis. University of Medicine and Dentistry of New Jersey: Piscataway, NJ, 1990.
- (51) Upton, A. C.; Kneip, T.; Toniolo, P. *Ann. Rev. Public Health* **1989**, 10, 1–25.
- (52) Fenske, R. et al. *Am. Ind. Hyg. Assoc. J.* **1986**, 47, 764–70.
- (53) Pierce, T. *Ann. AGCIH* **1985**, 12, 331–37.
- (54) Estimating Exposures to 2,3,7,8-TCDD; U.S. Environmental Protection Agency: Washington, DC, 1988; EPA-600/6-88-005A.
- (55) Preparation of Soil Sampling Protocol: Techniques and Strategies; U.S. Environmental Protection Agency: Washington, DC, 1983; EPA-600/4-83-200.
- (56) Kimbrough, R. D.; Falk, H.; Stehr, P. *J. Toxicol. Environ. Health* **1984**, 14, 47–93.
- (57) Awang, S. T. *Nucl. Chem. Waste Manage.* **1987**, 7, 95–98.
- (58) Pao, E. M. et al. In *Home Economics Report #44*; U. S. Department of Agriculture: Washington, DC, 1982.
- (59) Osborne, M. R.; Crosby, N. J. *Benzopyrenes*; Cambridge Monographs on Cancer Research; Cambridge University Press, Cambridge, U.K., 1987.
- (60) National Research Council Subcommittee Report on Biologic Markers in Pulmonary Toxicology. National Academy Press: Washington, DC, 1989; p. 1437.



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