# Biomonitoring of Industrial Pollutants: Health and Policy Implications of the Chemical Body Burden

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Biomonitoring of industrial chemicals in human tissues and fluids has shown that all people, not just those working in or living near major pollution sources, carry a "body burden" of synthetic chemicals in their blood, fat, mother's milk, semen, urine, and breath. In March of 2001, the Centers for Disease Control and Prevention (CDC) presented its National Report on Human Exposure to Environmental Chemicals, the first of a planned series of annual studies of the types and amounts of industrial chemicals that Americans have in their blood and urine.[1]

An immense chemical industry that grew rapidly after World War II provides materials now used in virtually every sector of commerce and in every home in the United States. More than 70,000 individual industrial chemicals are registered with the Environmental Protection Agency for commercial use; of these, some 15,000 are nonpolymeric chemicals produced in quantities greater than 10,000 pounds per year, and 3,000 to 4,000 have production volumes over one million pounds annually.[2] Only a very small fraction of these substances has been characterized for biological activity or human toxicity.[3] Meanwhile, an average of 2,300 new chemicals are introduced onto the market each year.[4] Several classes of chemicals, including the organochlorines and heavy metals, are the object of considerable public health and regulatory concern because of their tendency to persist in the environment, bioaccumulate and bioconcentrate in food webs, and disrupt biological processes at low doses.

Residues of industrial chemicals can now be found in air, soil, water, and food webs in the most remote reaches of the planet.[5,6] All humans are now exposed to synthetic pollutants in drinking water, air, and the food supply,[7,8] as well as in consumer products and home pesticides.[9,10] Some of these chemicals resist metabolism and excretion and therefore accumulate in body tissues. The quantity of an exogenous substance or its metabolites that accumulates in an individual or population is defined as a "body burden." The toxicology of individual industrial chemicals is covered in textbooks[11,12] and in government

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reports, such as the Agency for Toxic Substances and Disease Registry Toxicological Profile Series.[13] In this article, we comment on biomonitoring and its importance for public health research and practice, and discuss research and policy issues raised by the existence of the universal chemical body burden.

## MONITORING THE CHEMICAL BODY BURDEN

Biomarkers of exposure, susceptibility, and effect are important for establishing causality and identifying mechanisms that link chemical exposure and adverse health outcomes.[11,12] An individual's body burden of a pollutant is estimated by measuring the concentration of that substance in one or more tissues.[14] Such measurements serve as indicators of recent or long-past chemical exposures.

Body burdens are complex and dynamic in a number of ways. First, tissue levels of a pollutant are not stable over time. The concentration at any one time reflects a dynamic balance between the amount taken in and the amount excreted or metabolized into another material. Many industrial chemicals, such as formaldehyde, benzene, and some pesticides, are rapidly excreted or metabolized, producing a negligible long-term body burden. Others have long or intermediate biological half-lives and therefore accumulate progressively in a person's tissues as exposures continue.[15] Tetrachlorodibenzo-*p*-dioxin, for example, has an estimated half-life in humans of seven years, and body burdens generally increase with age.[8] Body burdens are not distributed homogeneously within an individual, either. The partitioning of a pollutant among various tissues and fluids reflects the substance's relative affinity for water, fat, or mineral matrices; for example, polychlorinated biphenyls (PCBs), like other hydrophobic pollutants, accumulate in adipose tissue, and calcium-mimicking lead concentrates in bone.

The ability of chemical analyses to characterize the full range of contaminants is limited by technology and existing information.[14,16] Compounds can be identified only if they are present in concentrations above a detection limit (usually in the parts per trillion or billion). Moreover, routine analyses can identify only compounds that can be matched against a reference database of chemical signatures; novel or exotic compounds therefore remain unidentified in even rigorous analyses. Standards have yet to be developed for the vast majority of industrial chemicals and their environmental and metabolic byproducts, so that the population's body burden remains uncharacterized to a large extent. The adipose tissue of the U.S. general population contains 700 contaminants that have not been chemically identified and are considered likely to be exogenous, because they increase in number and concentration with the age of the individual from which the sample was drawn.[16]

## THE GENERAL POPULATION'S BODY BURDEN

The human body burden of specific industrial substances has been well-characterized in selected populations, including victims of chemical accidents;[17] workers in agriculture,[18] chemical[19] and incineration industries;[20] military personnel exposed to herbicides like Agent Orange;[21] and individuals exposed through contaminated food.[22]

A substantial body of research has examined chemical contamination of people with no special exposures. This work indicates that the general public bears a body burden of a diverse group of industrial chemicals and pesticides, presumably because of global contamination and universal exposure. A review of the literature, for example, shows that more than 190 synthetic organochlorines have been detected in the blood, adipose tissue, mother's milk, semen, breath, and urine of the general population of the United States and Canada.[23]

Most studies to date have focused on a few chemicals in relatively small study populations. We conducted a pilot study for a planned investigation of attitudinal and behavioral responses to information about one's personal body burden. We measured an extensive panel of more than 150 chemicals in the blood and urine of a convenience sample of nine normal subjects with no unusual exposures. The results (see Table) are consistent with the view that a body burden of phthalate plasticizers, dioxins, furans, PCBs, metals, and pesticides is a universal phenomenon. Chemical body burdens have been studied in several large surveys using nationally representative samples of the U.S. population. The National Health and Nutrition Examination Survey (NHANES II) examined the levels of lead and 36 pesticides and pesticide metabolites in the blood of a national sample of nearly 6,000 people ages 12–74 years from 1976 to 1980. Follow-up research in NHANES III and NHANES IV included other heavy metals and volatile organic compounds.[24] Savage and coworkers reported on pesticide levels in human breast milk in a broad geographic sample of the U.S. nursing mother population.[25]

From the early 1970s to 1992, the Environmental Protection Agency's (EPA's) National Human Adipose Tissue Survey estimated the general population's body burden of several hundred synthetic chemicals, using surgical and postmortem body fat specimens.[26] Al-

**Table. Detection of industrial chemicals in the blood and urine of nine human subjects from the general population**

| | *Total tested* | *Total found* | *Number of subjects with detectable residues* | *Average detected value* | *Detected range* | *Test detection limit* | *Units*[a] |
|---|---|---|---|---|---|---|---|
| Dioxins and furans | 17 | 15 | 9 of 9 | 26.0 | 15.7–36.6 | [b] | pg/g TEQ |
| PCBs | 77 | 52 | 9 of 9 | 5.5 | 1.5–10.9 | [b] | pg/g TEQ |
| Metals | 5 | 4 | 9 of 9 | | | | |
| Lead | | | 9 of 9 | 2.37 | 1.01–3.23 | [b] | µg/dL |
| Methylmercury | | | 8 of 9 | 9.11 | 0.63–25.9 | [b] | µg/L |
| Arsenic, inorganic | | | 1 of 9 | 21 | 21 | 10 | µg/L (urine) |
| Cadmium | | | 3 of 9 | 0.6 | 0.5–0.7 | 0.5 | µg/L (urine) |
| Chromium | | | 0 of 9 | | | 1.0 | µg/L (urine) |
| Organochlorine pesticides | 22 | 10 | 9 of 9 | | 615–3084[c] | [b] | µg/L |
| Organophosphate pesticides | 9 | 6 | 9 of 9 | 29.6 | 4.0–70.4[c] | [b] | µg/L (urine) |
| Phthalates[d] | 6 | 6 | 9 of 9 | | | | |
| Semivolatile organics[d] | | 78 | 9 of 9 | | | | |

[a]pg/g = picograms per gram of lipid in the blood or parts per trillion

[b]Detection limit varies among substances in this class

[c]Sum of all chemicals in this class

[d]Not quantified

µg/L = microgram per liter of whole blood or approximately parts per billion

µg/dL = microgram per deciliter of whole blood or approximately one-tenth parts per billion

µg/L (urine) = microgram per liter of urine or approximately parts per billion

PCBs = polychlorinated biphenyls

TCDD = tetrachlorodibenzo-*p*-dioxin

TEQ = toxic equivalent, scaled to 2,3,7,8-TCDD, expressed as the sum of all chemicals with an available TEQ conversion

NOTES: Subjects were a convenience sample of volunteer colleagues of the investigators. Fasting blood was drawn, iced, and sent with a 24-hour urine collection to the Midwest Research Institute (Kansas City, MO) for analysis. Semivolatile chemicals represent tentatively identified compounds as determined by a standard electronic chemical library. The mass spectra of each tentatively identified compound, manually verified against the identified library spectra, met the project-specific objective of 70%–100% forward/reverse fit. Nondetects were treated as zeroes in all statistical calculations. For polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans, TCDD equivalents (TEQs) were calculated based on the World Health Organization method.[2] The study was approved by the Institutional Review Board of the Mount Sinai School of Medicine for human subjects research. Details of the measurement methods and congener-specific data are available from the authors.

though that program has been criticized for lacking a standardized methodology and for using a sample of individuals that may not accurately reflect the nation's population, the program's results remain one of the most comprehensive available datasets on the general population's body burden. In the 1980s, another EPA program sought to characterize the public's "total exposure" by measuring a large number of industrial chemicals in human breath in a pilot study of 12 volunteers from New Jersey and North Carolina, and then in an expanded investigation of 188 Californians.[27,28] Another EPA analysis identified several dozen synthetic chemicals in mother's milk from 42 women in New Jersey, Pennsylvania, and Louisiana.[29]

In 1991, a committee of the National Academy of Sciences called for a national program to monitor blood samples from the general population for the presence of a list of target substances, based on a standardized protocol.[14] Subsequently, the National Center for Environmental Health, a division of the CDC, initiated the National Exposure Report program.[1] The first results from this program reported on the presence of heavy metals, phthalates, and several pesticides in a very large sample of the U.S. population, with data on the variability of contaminant levels by age, sex, and region. In coming years, the study will be expanded to address a larger list of about 100 substances.

A particular value of the CDC's national biomonitoring program is its capacity to establish reference ranges—descriptions of the concentration of a particular substance normally present in the general population. A reference range serves as a standard against which a public health laboratory can say that results for any group or individual are high, in a "normal" range, or low.[30] For well-studied pollutants such as lead,[31] selected pesticides,[32] dioxins, and PCBs,[33] good reference values already exist because large numbers of people have been studied using standardized methods. For most substances, laboratory methods have varied over time, and few nationally representative populations have been studied, providing no reference for interpreting biomonitoring data on a specific individual or cohort.

A lack of historical data for most pollutants and changes in analytical methods over time make results difficult to compare. As a result, tracking temporal trends in body burdens and exposures for most pollutants is difficult. If continued over the long term, CDC's biomonitoring program promises to address this problem. For some pollutants, however, there is good historical data available now; these indicate that the existence of an appreciable body burden of industrial chemicals is a recent phenomenon. For example, dioxins in preserved human tissue samples from preindustrial times are nondetectable or present at only a very small fraction of current concentrations.[34,35] It is also clear that levels of persistent organochlorines, the use and production of which were restricted in industrialized nations—such as PCBs, DDT, heptachlor, and some other pesticides—declined in adipose tissue and mother's milk in the 1980s and early 1990s, and then apparently leveled off.[36–38]

Data on the distribution of body burdens among age groups are also limited, and children are of special concern. Once persistent pollutants take up residence in human fatty tissues, there is no effective way to eliminate them. Women, however, excrete accumulated persistent chemicals into the fat of breast milk and, in smaller quantities, across the placenta into the fetus.[39,40] The developing infant is therefore exposed to these compounds during critical periods, particularly prenatally, when sensitivity to chemically induced disruption is high.[41] After weaning, children continue to receive substantial exposures because of higher intake rates of food as a fraction of body weight. With the exception of lead, there have been no comprehensive analyses of the chemical body burdens of children. A large national prospective longitudinal cohort study of American children has recently been proposed[42] to investigate the role of various risk factors, including early exposure to environmental toxicants, in a variety of developmental outcomes such as birth defects, cognitive impairment, developmental and behavioral abnormalities, immune dysfunction, and childhood cancer. A large-scale study of pollutants in the milk of U.S. mothers has also been proposed.[39]

## PUBLIC HEALTH AND RESEARCH IMPLICATIONS

Public health scientists and practitioners can use biomonitoring information for tracking, control, and treatment. The traditional purpose of biomonitoring programs is to assess the health risks of occupationally or environmentally exposed individuals. Because body burdens integrate exposures that occur across time and environmental media and reflect the accumulation of pollutants after metabolic and partitioning processes, biomonitoring data can also play a critical role in identifying novel hazards and high-risk populations, tracking trends in human exposure, and characterizing exposure levels that pose health hazards.[14]

From a public health perspective, the critical question raised by the existence of a universal chemical body burden is whether low-level chemical exposures can cause large-scale impacts on the health of the general population. Even in the absence of new external exposures, accumulated pollutants serve as a reservoir for continuing internal doses[43] and transfer to the developing child in utero and via nursing.[44] The demonstration of biological effects at very low levels of exposure[45–47] suggests that two toxicological axioms—all chemicals have thresholds below which they cause no adverse effects, and therefore that "the dose makes the poison"—should be reevaluated. Findings in developmental toxicology indicate that extremely small doses of some substances, particularly during critical developmental periods, have the potential to cause permanent disruption.[48] Furthermore, natural endogenous chemicals, including hormones and neurotransmitters, are frequently present at concentrations high enough to cause biological effects; xenobiotic exposures to substances that act through the same or related mechanisms may therefore take place in an organismal milieu that is already at the threshold for biological disruption.[49] These considerations suggest that if thresholds do exist, they are sometimes so low as to be irrelevant from an environmental health perspective.

Evaluating the possibility of a link between universal chemical exposure and health impairment poses a major challenge to public health scientists. When the exposed population is the general public, there is no unexposed or even less exposed group to serve as a

reference; it is therefore impossible for the existence of chemically induced effects at the low end of the general population's exposure distribution to be directly inferred epidemiologically.[50] It is possible to compare groups from the general population that differ slightly or moderately in the magnitude of their exposures to study the hazards of elevated exposures. When the differences between exposed and reference groups are small—as they must be for findings to be relevant to background exposures—very accurate characterizations of exposure and effect are required. Unfortunately, relevant impacts (e.g., deficits in immunity, fertility, or cognition) are often subtle, difficult to quantify, vary naturally within the population, take years to be expressed, and reflect exposure to chemical mixtures, nonchemical agents, and other confounders, including socioeconomic and related variables. Epidemiology is therefore quite limited in its ability to untangle the causal webs that link long-past, complex exposures to subtle forms of population health damage. As a result, conclusive and specific causal links are likely to be established between universal exposures and health impacts in the general population only in rare cases, even though effects that escape detection could be of considerable public health significance.

Determination of health impacts at background doses requires an integrated approach to evidence from diverse sources, and biomonitoring data can play a critical role in this strategy. For example, body burden measurements automatically account for differences in metabolism and excretion, increasing confidence in the extrapolation of toxicity data across species and individuals.[8] Biomonitoring therefore allows comparisons between well-controlled studies on laboratory animals and the general public's exposures. Studies of this type have found that current "background" body burdens of dioxins, PCBs, and several other well-studied organochlorines in humans are at or near the range at which adverse effects occur in laboratory animals. For example, the body burden of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans in the average American adult has been found to be 8–13 parts per trillion, expressed as tetrachlorodibenzo-*p*-dioxin equivalents (TEQ);[51] when dioxin-like PCBs are included, the total TEQ in blood lipids in the 1990s is 25 parts per trillion.[8] In comparison, a dioxin dose that produces a level of just 5 parts per trillion in blood lipids of pregnant rats reduces sperm density by 25% in the male offspring. At a maternal body burden of 13 parts per trillion, puberty is delayed, and penises and ducts in the testes are smaller.[52] Other animal studies have established endocrine, neurobehavioral, and reproductive system impacts of other persistent chemical pollutants in the range of the general population's body burdens.[51,53–55]

Body burden data can also facilitate geographic evaluation of chemical exposures and its relation to health impacts. For example, causal links have been established between consumption of organochlorine-contaminated fish from the Great Lakes and large-scale reproductive, developmental, endocrine, and immunological dysfunction in birds, fish, and mammals.[56] Body burdens of bioaccumulated pollutants are only about 5–10 times higher than in otherwise identical inland populations from the same region that eat less contaminated fish and do not manifest the same impacts.[56] These data suggest the possibility that subtle effects may also occur in the comparison population and other wildlife populations in locations around the world. The body burdens of dioxins and PCBs observed to cause developmental impairment in Great Lakes fish and wildlife range from 5 to 1,000 parts per trillion in the embryo (TEQ); the lower end of this range includes the levels found in the general human population.[56,57]

Body burden data have also emerged as an important biomarker for epidemiological inference. Effects with decades-long latencies often make direct assessment of relevant exposures impractical. Body burdens, however, provide a present indicator of long-term exposure for persistent chemicals, allowing a putative link between the risk of disease and tissue levels of one or more pollutants to be studied; for nonpersistent or nonbioaccumulated substances, tissue and fluid levels indicate the extent of recent exposures. Body burden data are particularly useful for examining developmental impacts: maternal body burdens of bioaccumulated substances provide a biomarker of the fetus's in utero exposure, and contaminant levels in mother's milk are a biomarker of exposure through nursing. A number of studies have used body burden data to establish that exposure to dioxins and PCBs early in life is associated with reduced cognitive ability, shortened attention span, thyroid hormone disruption, and compromised immune defenses. In these studies, women and their children drawn from the general human population have been studied; the offspring of mothers at the higher end of the reference range for PCB and dioxin body burden have been found to have significantly greater risks of developmental impairment than those in the lower end, even after controlling for a wide variety of confounders.[58–63] Careful analysis has allowed the relative roles of in utero and lactational exposure to be evaluated, with most studies finding prenatal exposures to be more important than those incurred during breastfeeding.[58–60]

## IMPLICATIONS FOR HEALTH POLICY AND EDUCATION

The existence of a universal, low-level chemical body burden raises questions about the adequacy of current environmental health policies. Regulations in most industrialized nations allow virtually unlimited production and use of synthetic chemicals; discharges of some substances from individual facilities are limited to levels predicted to produce "acceptable" levels of local contamination and exposure. The general population's body burden, however, indicates that even very small releases of persistent, bioaccumulative substances can build to significant levels over time. Furthermore, the focus on single substances, single facilities, and local environments takes no account of the total global pollution burden produced by thousands of permitted activities occurring simultaneously.

Policies could more effectively reduce the total environmental load and human exposure burden by seeking to diminish the production and use of all potentially hazardous chemicals in a systematic, prioritized fashion.[23] Sweden, for example, has established a national program to reduce its overall reliance on synthetic chemicals; the strategy requires a phase-out by 2015 of substances that are persistent, bioaccumulative, carcinogenic, mutagenic, or toxic to the reproductive or endocrine systems. This program will also reverse the burden of proof, so that substances that have not been toxicologically evaluated must be withdrawn from the market by 2010.[64] The European Parliament has voted for the implementation of an almost identical program throughout the European Union.[65] Chemical management programs should also include the rigorous and ongoing evaluation of alternatives, so that one severe hazard is not replaced with another, and the most sustainable techniques are used to fulfill society's needs.

The complexity of the human body burden and the limits of epidemiology have important implications for the use of science in environmental and health policy. Some commentators, citing the absence of conclusive and direct epidemiological demonstrations of causal linkages, have concluded that "background" levels of chemical exposure are not causing health damage in the general population and that preventive measures are unnecessary.[66] The limitations of epidemiological analysis make such a standard of proof difficult or sometimes impossible to achieve. Insistence on conclusive causal links that can be established only with great difficulty prevents timely action to reduce health risks, even in the face of a suggestive body of evidence that chemical exposure has the potential to cause long-term, global health impairment. To demand proof actually requires large-scale health damage to occur in the human population before preventive action can be taken. Policies of this type conflict with the "do no harm" ethical basis of health and medical practice.

The limits of environmental health science have led to an increasing acceptance and application in environmental law of the precautionary principle: environmental damage should be anticipated and prevented in the face of uncertainty by avoiding potentially damaging activities whenever possible.[67] Precaution is entirely consistent with the primacy of prevention among the principles of public health practice. Precautionary action implies a progressive effort to implement safer products and processes, reducing the production and use of all potentially hazardous chemicals. Such a program would almost certainly reduce the burden of toxic substances in the environment and in human tissues.

Biomonitoring can play an important role in health education by providing workers and citizens with knowledge of their personal chemical exposures. When individuals understand that their bodies are contaminated and identify the sources and pathways of exposure, they may modify their diet or change their residence or occupation. They may ask for health screening and medical advice about their risk factors, and health care practitioners should be trained and informed to respond to these queries. Awareness of the universal nature of such exposures may lead individuals to take political action and seek systematic reductions in the release of pollutants to the environment. Information on the universal chemical body burden may therefore be a useful tool in environmental protection and the health education of the general public.

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