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Biomonitoring Basics

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Michael A. Kamrin, Ph.D.
Professor Emeritus
Institute for Environmental Toxicology
Michigan State University

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7525 PRESIDENTIAL LANE, MANASSAS, VA 20109 PHONE: 703-331-5500/202-737-0337

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Biomonitoring in brief

Summary

Biomonitoring is a scientific technique for assessing human exposures to natural and synthetic compounds in the environment. It is based on analysis of human tissues and fluids and provides the only direct method of determining if people have been exposed to particular substances, what the magnitudes of their exposures are, and how these may be changing over time. Biomonitoring has become a more useful tool in recent years as the result of advancements in the capability to measure more and more minute amounts of chemicals in the human body.

With these new capabilities, the U.S. Centers for Disease Control and Prevention (CDC) has started an ambitious biomonitoring program that is aimed at increasing understanding of current and past exposures to natural and synthetic compounds in our environment. This program will provide baseline information that can be used to identify which compounds are present and in what amounts, to determine background levels of these compounds and, after repeated monitoring, to detect trends in exposures.

Because of the extensive resources needed for biomonitoring, only a limited number of people and compounds can be studied and only a few types of body fluids examined. In addition, because studies are done at just a few points in time, the results cannot provide information about how often individuals have been exposed, for how long or to what quantities of each substance. Thus, these data on body levels cannot be used to determine the doses people are exposed to on a daily basis.

Because almost all toxicity studies are based on the relationship between daily dose and adverse effect, and biomonitoring cannot provide dose information, measured body levels generally cannot be used to assess risk. Thus, the presence of a substance in the body, at any level, cannot be interpreted to mean that adverse effects are likely to occur.

Although it cannot be used to assess risk, exposure information collected through biomonitoring can be beneficial in a number of ways. It can identify environmental substances that have increased in concentration to levels that can be detected in humans and thus may contribute to the discovery of new sources of such compounds. Biomonitoring results can be used by physicians to diagnose individuals who have been exposed to excessive amounts of environmental chemicals, thereby making it possible to design appropriate interventions and treatments. Trends in monitoring data can be very useful in evaluating the success of policies designed to reduce the levels of particular compounds in the environment.

Scientists can also use biomonitoring data to provide direction for future research. These data may suggest the need for additional studies on the toxicity of certain substances and the environmental movement of others, as well as provide guidance for refining existing exposure estimates based on traditional, indirect exposure assessment methods. As a result of the CDC studies and others of their kind, public health experts may be better able to focus their efforts on substances that are present at the highest levels, rather than on those that are not detected or are only found at very low levels.

Biomonitoring defined

What exactly is biomonitoring?

Biomonitoring is a scientific technique for assessing human exposures to natural and synthetic chemicals, based on sampling and analysis of an individual's tissues and fluids. While blood, urine, breast milk and expelled air are most commonly measured, hair, nails, fat, bone and other tissues may also be sampled. This technique takes advantage of the knowledge that chemicals that have entered the human body leave markers reflecting this exposure. The marker may be the chemical itself. It may also be a breakdown product of the chemical or some change in the body that is a result of the action of the chemical on the individual. For example, alterations in the levels of certain enzymes or other proteins may serve as markers; so too might modifications of normal body processes, such as the transfer of oxygen to tissues.

The levels of natural and synthetic chemicals detected through biomonitoring are sometimes referred to as body burdens. This is a misleading term in that it suggests that the detection of a substance always means that it is causing adverse effects. However, biomonitoring only measures exposure; it does not provide information about toxicity or risk. Indeed, many natural chemicals, such as the metal manganese, found in tissues and fluids are essential for the proper functioning of the human body.

Perhaps the most important strength of biomonitoring is that it is the only technique that can provide a direct measure of the exposure of human individuals and populations. However, because it requires a great deal of resources, only a relatively small number of individuals and compounds can be monitored. This, in turn, limits the amount and applicability of the analytical data collected.

In the absence of biomonitoring, exposure assessments are performed indirectly -- based on a combination of: (1) measurements of concentrations of chemicals in the environment, e.g., in soil, water, or food, and (2) estimates of human behaviors, e.g., food consumption or time spent at various activities. This indirect approach has several drawbacks. First, environmental analyses are typically limited in both space and time, i.e., concentrations are known for only limited numbers of places at a few times. Second, human behaviors are quite variable, and this adds significantly to the uncertainties in the calculations. Due to these limitations, it is difficult to know how accurately such indirect assessments reflect human exposures.

In addition to being a direct measure, biomonitoring has the advantage that it integrates, or adds together, exposures from multiple sources, e.g., air, water, and food, to provide a reflection of total exposure. Thus, it is a measure of total exposure by all routes and from all sources.
This strength of biomonitoring can also be seen as a limitation, because this automatic integration over routes and sources means that it is not possible to determine the

relative contributions of individual sources, e.g., fish consumption, to the total exposure. Another limitation is that biomonitoring only provides exposure information at one point in time. Thus, this technique cannot provide information about the time course of exposure, that is, whether it occurred as a result of one simple exposure, multiple independent exposures over a long period of time, continuous exposure over time or some combination of these.

Because of these limitations, biomonitoring by itself cannot provide information about either the likelihood or magnitude of future exposures. This is true even if a series of fluid and/or tissue measurements are performed over a significant time period, because a number of factors, e.g., possible changes in environmental concentrations, can influence the measured levels.

Substances measured

What kinds of substances are measured by biomonitoring?

Biomonitoring may be used to assess the levels of any chemicals, natural or synthetic, that are present or that have been present in the environment. Natural chemicals that have been the subject of biomonitoring include those found in the earth's crust, such as the elements lead and arsenic, as well as a large variety of more complex compounds that are part of the food that we eat, the water that we drink and the air that we breathe. These complex chemicals include substances that are a part of a number of plants and animals and that have biological activity, including natural pesticides, carcinogens, and hormonally active chemicals.

Synthetic (i.e., manufactured) chemicals, often the focus of public concern, include a large range of compounds that have been or are being manufactured for a variety of applications. Also included are the substances that are produced as by-products of the synthesis and use of these compounds. In the modern world, synthetic chemicals are a part of every aspect of human life; they are critical to preventing and treating disease, to transportation, to agricultural production and to the many consumer products used for supporting the standard of living we enjoy. Therefore, it is not surprising that many of these find their way into the soil, air, water and food and thus ultimately into the fluids and tissues of individuals.

Biomonitoring is best at detecting chemicals that persist in the body, i.e., those that are not rapidly broken down and/or excreted. Examples of such persistent substances include the metals lead and arsenic and a number of synthetic organic chemicals, such as PCBs and DDT. These chemicals are often found through biomonitoring not only because they persist in the human body, but also because they remain in the environment for long periods of time after they are released. Thus, exposures to these substances can occur continuously over long periods of time. Because of the combination of environmental and biological persistence, they are often found in humans at higher levels than other chemicals, even those that may be produced or used in much higher amounts. However, even for persistent chemicals, both natural and synthetic, body levels measured by biomonitoring are generally very low, typically in the parts per million (ppm), parts per billion (ppb) or parts per trillion (ppt) range. If one ppm was expressed as time, instead of as concentration, it would be the equivalent of 1 second in

11.5 days; similarly, 1 ppb would be equivalent to 1 second in 31.7 years, and 1 ppt would be equivalent to 1 second in almost 32,000 years.

One situation in which high levels of exposure may occur is from the ingestion of foods containing significant amounts of environmental chemicals. This may happen if there is bioaccumulation and biomagnification of the chemical as it is passed up the food chain from organism to organism, e.g., from very small creatures up to large fish. Higher levels of chemicals in food may also occur as a result of unusual environmental conditions, e.g., extreme climatic conditions. For example, certain fungi that make mycotoxins may be produced on grain in greatly increased amounts when the weather is unusually hot and damp for a long period of time.

In sum, biomonitoring is a way of measuring which substances humans have been exposed to and the relative amounts of exposure to those compounds. This technique detects both naturally occurring and synthetic substances. Generally, the ones that are detected at the highest levels are environmentally and biologically persistent or are present in the environment in unusual amounts because of special conditions.

How performed

How is biomonitoring performed?

The process of biomonitoring involves three steps: (1) selecting who will be monitored, as well as when and where, (2) collecting tissue and/or fluid samples, and (3) deciding which chemicals to study and analyzing for those chemicals in the samples that are collected. This is a complex and expensive process, especially if the goal is to obtain results that reflect how body levels vary by age, sex, ethnic group, geographical location, and state of health of the individual. Biomonitoring also depends on the ability of analytical chemists to detect minute amounts of chemicals, an ability that has increased significantly in the past decade. Thus, it is not surprising that biomonitoring efforts in the U.S. have been limited.

In recent years, however, the U.S. Centers for Disease Control and Prevention (CDC) has embarked on an ambitious program of monitoring. In 1999, the CDC collected samples from more than 4,000 people in about a dozen locations and analyzed these for twenty-seven chemicals, comprising metals, organophosphate pesticides, tobacco smoke and phthalates. Following this, in 1999-2000, the CDC expanded the study to include a total of 127 chemicals, although the numbers of people and locations involved were about the same as previously. Even though a fairly large number of people and locations were included in these investigations, the results of the studies can only provide reliable national averages rather than detailed information about specific sectors of the population.

Because of resource limitations, all of the CDC tests were performed using blood and/or urine samples, even though sampling other fluids, such as breast milk, or certain tissues might have provided additional significant information. For example, studies of breast milk levels can provide specific data on which chemicals breast-fed children are ingesting and in what amounts. This can be especially useful information for compounds, such as DDT, for which international experts have estimated acceptable maximum levels in breast milk. For another example, studies of metals, such as mercury, in hair can provide long-term rather than instantaneous exposure information, because the mercury is incorporated into the hair as it grows. Thus, the levels at the tips of the hair often represent mercury exposures a year or more prior to the time the test is taken, while levels in the hair nearer the scalp reflect more recent exposures.

The actual analyses are quite straightforward in most cases, as they are based on commonly accepted laboratory techniques. However, they do generally require sophisticated analytical instruments and techniques, because it is only the application of very sensitive test methods that provides the opportunity to detect the very small amounts of many of the environmental chemicals found in humans. These special tests cannot be performed by the medical laboratories that routinely do the blood and urine analyses ordered by doctors. Even with analytical advances, uncertainties may arise when measured levels are near the minimum levels that can be detected (limit of detection) or in situations where the analysis for a particular chemical is very difficult or has not been validated. In addition, there may be questions about which form or combination of forms is most appropriate to measure in cases where a chemical occurs in more than one form.

In sum, biomonitoring of compounds present in the general environment is a complex undertaking, requiring a great deal of skill and resources. Because of all of these limitations, even the largest current studies may not provide answers to many of the critical exposure questions, such as exactly which compounds are present in human tissues and fluids, how the levels of each chemical vary in particular segments of the population and at specific locations, and how these levels change over time.

What about exposure

What can be learned about exposure from the results of biomonitoring?

As indicated previously, biomonitoring provides a measure of the exposures to natural and synthetic substances in the various environments in which humans live. Until recently, biomonitoring was used mainly in occupational and a limited number of clinical settings. In the workplace, this approach provides information about workers who have received higher than acceptable exposures and thus need to change their environment and/or behaviors. Clinically, biomonitoring can be used in identifying specific individuals with high exposures, e.g., people exposed to large amounts of arsenic. This information can be used in deciding which medical interventions or treatments may be appropriate.

The extensive use of biomonitoring to assess general population exposures to chemicals in the outdoor and indoor environments is much more recent and is designed to accomplish a number of aims. Two of the main goals are to determine: (1) which chemicals are present at high enough levels to leave traces in the human body, and (2) the relative levels of these compounds. Since such biomonitoring has just begun, the early results are most useful for establishing baseline levels of each chemical, against which to compare future monitoring results. Such comparisons can identify trends in exposures and help to assess the success of steps that have been taken to reduce the amounts of particular chemicals in the environment. For example, the success of campaigns to reduce exposures to secondhand smoke can be assessed in this manner.

In addition, population biomonitoring may be helpful in identifying compounds whose levels in the environment have increased to the point that they can be detected in human fluids and tissues. These data often suggest that there are sources of this chemical that have not been identified or that knowledge about the environmental movement of these compounds is faulty. Moreover, the identification of these chemicals may be accompanied by the recognition that data on the possible adverse effects of these compounds is limited. These outcomes are likely to lead to additional research on sources, environmental distribution and toxicity of the newly detected compounds.

Further, if the monitoring is done on sufficiently large and diverse groups of individuals, it may be possible to identify specific sectors of the population that have significantly higher exposures to a particular chemical than does the general populace, e.g., urban dwellers may have higher exposures to components of automobile exhaust. This information, in turn, may help to identify sources of these chemicals and, if the levels are of public health concern, to develop interventions to reduce future levels of these compounds in humans.

Finally, general population monitoring results may be useful in extending the clinical applicability of such data, as they can be used to establish reference levels for a much greater number of chemicals than are currently known. Such reference levels can be used by physicians to assess whether individuals have unusually high exposures to a substance, and thus the appropriateness of particular medical interventions or treatments.

In sum, biomonitoring provides exposure information that can be used in a number of ways. These data help in understanding which chemicals are in the environment and the relative levels of each, how these levels change over time, and which sectors of the population may have unusually high exposures to particular compounds. As a result of this understanding, it may be possible to assess the effectiveness of steps taken to reduce exposures, to identify new research that is needed and to help physicians diagnose and treat patients who may have had unusually high exposures to particular substances.

What about risk

What can be learned about risk from the results of biomonitoring?

Whether a chemical found in the body poses any risk depends on two factors: (1) the magnitude, time course, and route (ingestion, inhalation or dermal contact) of the exposure, and (2) its toxicity, i.e., what, if any, adverse effects are associated with this type of exposure. Risks can occur if people are very highly exposed for a short time, less highly exposed for a long period of time, or exposed at lower levels to compounds with high toxicity. Thus, knowledge of both toxicity and the characteristics of the exposure is critical in assessing the possible risk.

Since biomonitoring provides only data on exposure, it cannot be used by itself in assessing risk. Monitoring data must be combined with toxicity data if risk estimates are to be calculated. However, it is important to realize that most toxicity data are generated from studies of laboratory animals, usually rats and mice, that are exposed to chemicals in their diet at the same levels every day (often for a lifetime). The results of such research are used to provide estimates of the levels in the diet required to cause adverse health effects in the animals. One problem in combining such results with biomonitoring data is that the relationship between the amount of a chemical in the diet and the amount in fluids and tissues is a complex one. Thus, unless adequate toxicokinetics data are available, it is very difficult to compare the dietary levels used in laboratory experiments to fluid and/or tissue levels measured in biomonitoring studies.

A second problem in combining available toxicity data with exposure data from biomonitoring is that the monitoring results generally reflect the fluid and tissue levels at one instant in time and do not provide information about the time course of the exposure. The monitoring results gathered at one point in time cannot be compared to the toxicity values generated from daily administration of compounds to experimental animals. As a result of these two problems, there is no easy way to use biomonitoring data to assess risk, even if the toxicities of the chemicals being monitored are well understood.

Biomonitoring data and toxicity data can be combined only if scientists have established a connection between particular adverse effects and the levels of a specific chemical in body fluids or tissues. The best example of this is research that has demonstrated the relationship between blood lead levels and neurological problems in young children. Because this information is available, the biomonitoring of children who are likely to have excessive exposure to lead, e.g., children living in older housing with peeling paint, can be used to identify those at risk and thus to develop approaches to reduce exposure and the incidence of adverse effects.

In sum, biomonitoring provides only one part of the data needed to assess risk—it cannot be used as a surrogate for risk. Even if extensive toxicity data for a chemical are available, they are almost always in a form that is difficult to combine with the biomonitoring-generated exposure values to assess risk. It is only in a small number of special cases, such as that of lead, that inferences about risk can be made readily from biomonitoring data.

Unfortunately, if individuals do not understand the limitations of biomonitoring in providing risk information, they may take steps to reduce exposures that increase rather than decrease their overall risk. A good example is mothers refraining from breast feeding when informed that certain chemicals have been found, or are likely to be found, in their breast milk. In almost all cases, the benefits of breast feeding outweigh any possible risks from these chemicals—a conclusion that is reflected in the advice given to nursing mothers by public health authorities.

Future directions

What are the future directions of biomonitoring?

Biomonitoring of large numbers of chemicals in representative human populations is just beginning. In these early stages, the aim is to assess the current levels of natural and synthetic chemicals in human tissues and fluids and to provide the data for decisionmaking about future research needs. The information that is being gathered will be used mainly to: (1) establish baseline and reference levels for environmental chemicals, (2) identify chemicals for which appropriate toxicological and environmental data are lacking, and (3) refine future biomonitoring efforts.

The results of the biomonitoring studies will be used to establish background levels against which to compare future monitoring results. As more chemicals are added to the biomonitoring studies, a broader picture of the characteristics of any exposures that are occurring can be developed. In addition, the impacts of various policies on these exposures can be evaluated. Further, the background levels obtained can serve as reference values for use in identifying individuals who may be experiencing above normal exposures and who may benefit from medical intervention or treatment.

Another outcome of biomonitoring is that it may reveal the presence of compounds that are not expected and for which limited toxicological and/or environmental fate data are available. If the levels of such substances are high enough, this information is likely to lead to increased research on the properties and effects of these compounds.

The results of current biomonitoring efforts will be used to refine future studies. Such data will reveal which compounds are present at the highest levels and thus are likely targets for future studies, as well as those that are not detectable or are detected at such low levels that future monitoring is unlikely to useful. These results may also identify specific segments of the population that appear to be experiencing the highest exposures and so may be appropriate targets for greater attention in the future. These further studies will not only refine our knowledge of body levels but also will address the question of which sources are the most significant contributors to the measured levels.

In summary, the results of biomonitoring can help to suggest which environmental compounds are of most importance, what the background and reference levels for these compounds are, and which segments of the population may be the most highly exposed. Each of these outcomes will lead to further study aimed at refining estimates of exposure, identifying sources, identifying population segments most highly exposed, and assessing the impacts of steps taken to reduce exposure. Thus, biomonitoring can contribute to research that alerts scientists, regulators, and the public to possible risks and also allays fears that might arise from the knowledge that large numbers of natural and synthetic chemicals are present in our bodies.