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Making Sense Of Biomonitoring

New tool for interpreting data is based on established safe doses for chemicals

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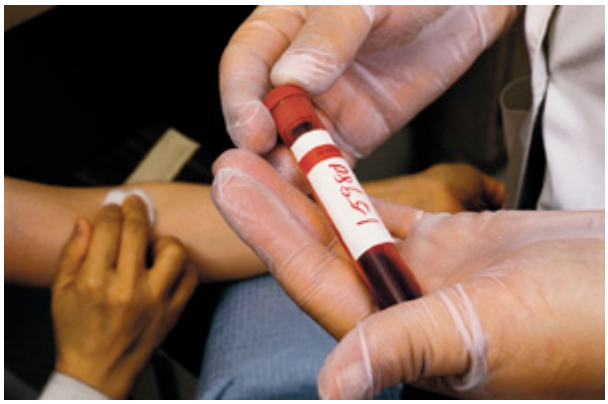
In an ideal world, scientists would be able to monitor industrial chemicals found in people's bodies and predict the health implications from any level of exposure to the substances. At the same time, they would be able to provide solid information about risk for companies, regulators, and the public to act on.

But scientific understanding isn't that far developed. Analytical tools are becoming more and more sensitive and have the ability to detect increasingly minuscule amounts of chemicals in blood, urine, or breast milk. Data from these sorts of analyses, collectively called biomonitoring, show that people's exposure to many synthetic chemicals is widespread.



Getty Images

Detect Improved analytical techniques allow the screening of blood and other bodily fluids for very low levels of industrial chemicals.

This means that the public has become more aware of the bodily burden chemicals have, and the government is helping in this regard. The Centers for Disease Control & Prevention (CDC) is analyzing blood and urine from thousands of U.S. residents for hundreds of industrial chemicals—including pesticides, perfluorinated compounds, and phthalates—as part of the National Health & Nutrition Examination Survey.

Investigations by journalists also are fanning interest. Nearly three years ago, the Oakland Tribune in California ran an award-winning series of articles revealing that the youngest member of a family of four, a 20-month-old toddler, had the highest level of polybrominated diphenyl ether flame retardants in his blood. *National Geographic* delved into the issue in October 2006 with an in-depth article by self-described "journalist-as-guinea-pig" David Ewing Duncan, who subjected his bodily fluids to a battery of analyses. In October 2007, CNN aired "Planet in Peril," a special that included a segment featuring reporter Anderson Cooper getting his blood screened for scores of industrial chemicals.

These news reports all raised a similar alarm: Many of the chemicals detected in people through biomonitoring can cause cancer or other health problems. But all of those reports also left the key question unanswered: What do the levels of toxics detected mean for the health of the individuals tested?

This question did not remain unanswered because of omissions by the reporters, but for a more worrisome reason: Scientists simply don't know the answer.

In a 2006 report, the National Research Council stated that the ability to detect a chemical in humans often exceeds the ability to determine whether that substance causes a health risk or to evaluate how a person is exposed to it (C&EN, July 31, 2006, page 38). For instance, the toddler in the *Oakland Tribune* series had 838 parts per billion of polybrominated diphenyl ethers in his blood. Laboratory rats show behavioral changes with 300 ppb in their blood. But no one knows whether the little boy has or will develop health or behavior problems because of the flame retardants in his body.

"Our ability to measure has outstripped our ability to interpret data," says Richard A. Becker, senior toxicologist for the American Chemistry Council (ACC), a chemical industry trade group.

Now, chemical manufacturers have joined with a commercial toxicology laboratory and two government regulatory agencies, the U.S. Environmental Protection Agency and Health Canada, in an effort to make more sense of the level of chemicals found in people's blood or urine.

This effort revolves around the concept of "biomonitoring equivalents." A biomonitoring equivalent, Becker explains, corresponds to the blood or urine level of a chemical—or its metabolites—if a person is exposed to a safe dose of the substance.

Calculation of a biomonitoring equivalent starts with an established safe dose for a chemical. Perhaps the mostly widely known type of established safe dose for chemicals is EPA's reference dose. A reference dose reflects EPA's scientific judgment on the amount of a substance that people can ingest daily without harmful effects. The particular values come with a nagging burden of uncertainty regarding their relevance to people, however, because they generally are extrapolated from the results of tests on laboratory animals.

For years, health and environmental advocates have questioned whether a safe dose based on laboratory testing of rodents truly protects the public, including sensitive subpopulations such as infants and the elderly, from adverse health effects. These safe doses are, nonetheless, the starting point for the new effort to put biomonitoring data in context.

"We need something for interpreting biomonitoring data," says Sean M. Hays, president of Summit Toxicology, a Colorado-based consulting firm. "The biomonitoring equivalent is imperfect, but it's a logical first step,"

Summit Toxicology is doing a pilot project to develop biomonitoring equivalents for four chemicals. Sponsors of the work are EPA, Health Canada, ACC, the Soap & Detergent Association, the American Petroleum Institute, and two pesticide industry groups, CropLife America and Responsible Industry for a Sound Environment.

EPA has an established reference dose for each of the four chemicals in the pilot project. One of the

chemicals is acrylamide, a substance formed when starchy foods are fried, baked, or toasted. It's also a probable human carcinogen that can damage the human neurological system as well. Another is the pesticide 2,4-D, which is (2,4-dichlorophenoxy)acetic acid. Cadmium, an element classified as a probable human carcinogen, is the third. The fourth, toluene, is an industrial solvent that causes neurological effects.


CNN

Investigate CNN reporter Anderson Cooper had his blood analyzed for chemicals as part of the "Planet in Peril" special broadcast in late 2007

Robert S. DeWoskin of EPA's National Center for Environmental Assessment, which provides guidance and risk assessments for protecting human health and the environment, says biomonitoring equivalents hold promise for interpreting biomonitoring data. These interpretations, he says, will be done in the context of current health-based guidance values such as the reference dose.

"The question becomes, is this biomonitoring level of a chemical high enough to do damage if the chemical is at a site in the body where it can do some damage?" DeWoskin tells C&EN.

Biomonitoring equivalents can then be used as a screening tool to help risk assessors or an individual, in consultation with a physician, "initially determine whether or not there is need for concern or more definitive testing for internal levels or toxicity," DeWoskin says.

Hays, meanwhile, says biomonitoring equivalents are designed as "screening values for public health," not to determine the risk posed to a particular person. They could provide a tool for prioritizing chemicals for further study, he says.

For instance, biomonitoring data for a particular chemical might demonstrate that the population's blood or urine level of a chemical is orders of magnitude lower than the biomonitoring equivalent. In this case, Hays says, "there's not much likelihood of a public health risk" from typical exposure to the substance.

But biomonitoring equivalents have limitations. It "isn't a bright line" between a person who experiences a safe exposure and one who is at risk of health effects from a chemical, Hays says. In fact, even if the data show exposures to a chemical above its biomonitoring equivalent, "you can't say there's an increased risk" of health problems from exposure to the substance, Hays says.

Becker adds that you need a large body of data because "you wouldn't be able to draw a particular risk-based conclusion for an individual." For this reason, Hays tells C&EN, biomonitoring equivalents are not intended to be "personal diagnostic tools" and aren't the last word in interpreting biomonitoring data. "We're not trying to oversell these or make them more than they are," he says.

Environmental advocacy organizations are tracking the development of biomonitoring equivalents. Richard A. Denison, senior scientist with Environmental Defense, an advocacy organization with a history of working with regulators and companies, says he has "no problem" with EPA working with industry to increase scientific knowledge and the ability to interpret biomonitoring data. Nonetheless, he points out, chemical manufacturers have a vested interest in minimizing the significance of data showing that people are exposed to synthetic substances that no one expected would end up in their bodies.

"Clearly, biomonitoring is seen by the chemical industry as a major threat," Denison says. After all, for years chemical manufacturers argued that so many of their products did not pose a risk to humans because people presumably were not exposed to the compounds, Denison says.

The growing body of biomonitoring data has shifted this discussion, Denison says. Now, he tells C&EN, the industry is contending that although exposure is occurring, the tiny amount of synthetic chemicals in people's bodies doesn't matter.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Extrapolate EPA establishes safe daily human doses for chemicals based on tests in laboratory animals.

In a statement released in November 2007, ACC said: "The public should not be misled into thinking that the products of chemistry are inherently dangerous just because chemicals can now—through improvements in analytical chemistry—be detected at trace levels in people's blood or urine. Biomonitoring indicates presence. It doesn't mean there is a significant health risk."

Ted Schettler, science director for the advocacy group Science & Environmental Health Network, an advocacy group, says biomonitoring equivalents "are an attempt, I suspect, to create a framework to minimize concerns" about exposure to industrial chemicals. "Nothing is inherently dishonest" about the development of biomonitoring equivalents, he says. But what these numbers turn out to be will depend heavily on scientific assumptions and judgments made in the calculations, Schettler says.

Development of a biomonitoring equivalent for a chemical requires data on how the body absorbs, distributes, metabolizes, and excretes the substance. Biomonitoring tests may determine the level of the substance in the blood or urine. But what matters for determining health effects is the concentration of the compound in the tissue of specific organs, such as the brain, adrenal glands, ovaries, or testes, which the chemical can adversely affect.

In other words, Schettler explains, biomonitoring is a measure of how well the body has absorbed a

chemical, not how much of the substance is in the area of the body where a substance wreaks harm. Toxicologists refer to these as target organs.

Hays and EPA's DeWoskin, meanwhile, say the concentration of a chemical in blood in some cases is a good "surrogate" for the level in a tissue affected adversely by the substance, such as the brain or liver. There are exceptions, Hays adds. For example, cadmium can cause damage in the kidney, so using urine biomonitoring data would be better than blood-based data for developing a biomonitoring equivalent for this element.

Another problem with biomonitoring is that translating an established safe dose of a chemical into a biomonitoring equivalent such as parts per billion of a chemical in blood will call for expert judgments and assumptions, Schettler says. Calculations will involve educated guesses about how often people are exposed to the chemical, he explains.

For some chemicals, people exposed to different amounts of one chemical can end up with similar concentrations of the substance in blood, urine, or breast milk, Schettler says. A man who inhales a large dose of benzene while filling up a gasoline can, for instance, will end up with a high level of the chemical in his body. But over time, as his body metabolizes it, he eventually will have as much of the substance in his blood as a worker who is exposed to a small amount of benzene on the job every weekday, Schettler explains.

Schettler and Denison agree that a biomonitoring equivalent cannot differentiate whether a blood or urine level of a chemical is due to exposure to small amounts of a chemical over time or to a large one-time dose that the body is slowly clearing.

A large dose of a substance over a short period of time—called an acute exposure—may lead to different toxic effects than the same amount spread out over a longer time, which is referred to as a chronic exposure, Schettler says. Biomonitoring equivalents, he adds, would not account for this difference.

The peak level of a chemical in the body may be more relevant to an individual's chance of developing health problems than it is to how much of the substance is found in his or her blood or urine on average over time, Schettler says.

A partygoer who guzzles five beers in an hour, for example, is in greater danger of acute alcohol poisoning and will show a higher blood-alcohol content than one who drinks five brews over the course of five hours.

With toxicity, the plot is thick with many confounding factors. For example, whether a person is deficient in any vitamins or minerals is an important aspect in determining risk for adverse effects from chemical exposure, according to Schettler. So are social circumstances—such as access to regular medical care, he says.

Another confounding dynamic is that people are exposed to a mixture of chemicals in the environment that may interact, including synergistically or antagonistically. This may limit the usefulness of biomonitoring equivalents, Shettler notes.

Researchers are just now developing a foundation for biomonitoring equivalents. But this measure could have a strong impact on the public, its perceptions of chemicals, people's health, and chemical companies' bottom lines. These values could provide the public with some assurances that the amount of a particular toxic substance people have in their blood is of little worry. But if analyses, such as the National Health & Nutrition Examination Survey data, show an exposure exceeding a biomonitoring equivalent for a substance, regulators might be prompted to clamp down on the compound. Or this information could dampen the market for products containing it.

Despite these unknowns, biomonitoring equivalents show promise to the people, physicians, and

everyone else interpreting the onslaught of data about the many industrial chemicals that have found their way into their bodies.

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