

Biomonitoring is charting the public's exposure to many chemicals, but often the health effects are unclear

Pollution Gets Personal

After the World Trade Center towers collapsed on 11 September 2001, the world was gripped by the search for survivors. Researchers at the Centers for Disease Control and Prevention (CDC) raced to address an additional concern: the exposure of rescuers to potentially toxic smoke from the rubble. They took blood and urine samples from 370 firefighters, including those digging through the rubble at Ground Zero and those putting out nearby blazes. After examining the samples for dioxins, cyanide, and 100 other chemicals associated with burning buildings, they determined that the rescuers had not been exposed to dangerous levels. Although the team couldn't rule out all possible health effects, James Pirkle, deputy director for science at CDC's Environmental Health Laboratory, says the fast tests were "a huge help," eliminating the need for a lot of further studies.

What made the rapid findings possible were tremendous advances in methods of sampling human tissue for chemicals, called biomonitoring. Over the past decade, analytical techniques have improved so much that researchers can detect ever smaller concentrations of chemicals in a single blood sample. The largest effort is CDC's National Report on Human Exposure to Environmental Chemicals, an ongoing \$6.5 million survey that is now measuring about 145 chemicals in some 2500 people across the United States every 2 years. "It's critically important early intelligence about compounds that are getting into people," says Philip Landrigan of Mount Sinai School of Medicine in New York City.

Biomonitoring is hot. With lab costs down, environmental groups are commissioning their own analyses of chemical exposures. Last year, the Environmental Working Group (EWG) in Washington, D.C., released a report entitled *Body Burden: The Pollution in People* that examined the levels

of 210 chemicals in nine people. In April, the World Wildlife Federation tested for 101 compounds in 39 members of the European Parliament. The impetus is clear: Such studies can generate headlines and political



Clearing the smoke. Rapid sampling of rescuers alleviated some health concerns.

leverage. As a result of biomonitoring data, "we'll see sweeping changes in our system of public health safeguards," predicts Jane Houlihan, EWG's vice president of research.

But although biomonitoring can provide reams of statistics about the chemicals people are exposed to, it can't necessarily indicate whether such exposures are likely to make them sick. So while environmentalists herald biomonitoring as a valuable tool for precautionary action, chemical manufacturers worry that it will spark unjustified alarm and costly regulations that may not provide much real benefit to public health. "Industry sees a movement toward collecting a lot of biomonitoring data prematurely, before we know what to do with it," says Nancy Doerrer, scientific program manager at ILSI Health and Environmental Sciences Institute, an industry-funded group in Washington, D.C. What's becoming ever more obvious, researchers say, is a growing data gap: Although testing for a chemical can take just a few days, discerning its impact on health takes years, says Landrigan. "It's a real conundrum."

Going public

Public health researchers have long studied worker exposure to chemicals. Such testing was key in figuring out the toxicity of PCBs and dioxins, for example. But measurements

of actual exposures among, say, chemical plant workers don't translate easily to the average person, who encounters small concentrations through food, air, or skin.

Enter CDC, which in 1976 first looked at blood and urine samples of the general population and checked for environmental chemicals, including lead and a handful of pesticides. Examining the public for chemical exposure was "a fundamental change in mindset," says Joseph Thornton, a molecular biologist at the University of Oregon, Eugene. The same point is

hammered by environmental groups: Everyone is exposed to chemicals.

CDC's small testing program was massively expanded in the late 1990s to become the world's largest survey of chemical exposure among the general public. As part of the National Health and Nutrition Examination Survey (NHANES), CDC's biomonitoring results provide a guide to typical exposure to chemicals that pose a known or possible threat to health. Many are pesticides; others are ingredients in cosmetics, plastics, and other components of everyday life. Says Arnold Schecter of the University of Texas School of Public Health in Dallas: "CDC is providing a very careful look at the U.S., a nice snapshot."

Biomonitoring's strong suit is that it directly measures the amount of a chemical in bodily fluids or tissues. Those exposure data are much more relevant for risk assessments than are extrapolations from chemical concentrations in soil, air, or water. What you really want to know is not whether asbestos is in the walls but whether it's in your lungs, says

Schechter: “If you didn’t get it in your body, you don’t need to worry about health effects.”

Ideally, biomonitoring can help public health officials figure out what to worry about—and what not to worry about. But a caveat is that high levels aren’t necessarily dangerous, and typical levels aren’t necessarily safe. Other major factors relevant to health are how long the compounds persist in the body and the degree to which various groups are exposed. The large sample size of NHANES helps average out these variations.

What’s normal?

Early surveys were at irregular intervals, but CDC decided in the late 1990s to conduct an ongoing sample of the U.S. population every 2 years. All year long, CDC teams are taking four tractor-trailers to neighborhoods in 30 locations across the country, interviewing residents, performing exams, and sampling blood and urine.

The number of chemicals tested has jumped from 27 in 2001 to 116 in the most recent survey, released last year. Next year’s edition will include about 145. Costs of testing have dropped and speed has shot up, thanks to improvements in mass spectroscopy and other techniques, many of which were pioneered at CDC. “The analytical science has advanced just astronomically,” says Landrigan. Since the 1970s, the precision of lead measurements has increased dramatically, and instead of needing 10 milliliters of blood, only a drop is required. That means researchers can test for many dozens of chemicals in a single 10-milliliter blood

sample. More chemicals and more frequent testing mean they can spot trends sooner.

Biomonitoring showed its mettle early on when it tracked the success of a major public health intervention: the reduction of blood lead levels. When the United States and other countries set out to reduce automobile emissions, models had suggested that lead levels in children would decrease slightly as gas lead levels declined. Beginning in 1976, CDC began checking lead levels in children and adults. Although some questioned the expense of biomonitoring, recalls Landrigan, “the payoff was almost instantaneous,” by showing that the lowered lead level in gasoline was having a dramatic effect. In fact, biomonitoring revealed that blood lead levels declined about 10-fold more than expected between 1976 and 1980. These data were instrumental in the Environmental Protection Agency’s (EPA’s) decision to remove lead from gasoline more rapidly.

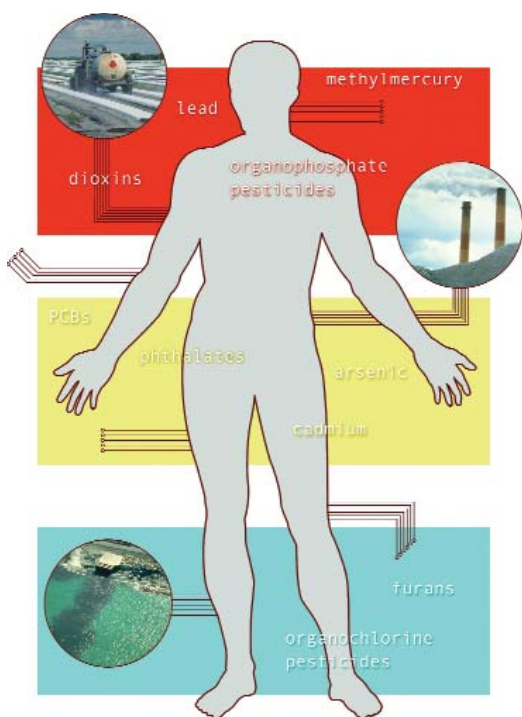
By determining typical exposures in the general population—called a reference range—researchers can better investigate concerns about cancer clusters or other apparently heightened disease rates. In 2001, for example, the state of Nevada asked CDC to help study leukemia rates in Fallon, Nevada. Of the 110 chemicals measured, they identified two, tungsten and arsenic, that were found in much higher concentrations among all residents—healthy and sick—than in the rest of the population. As a result, the National Institutes of Health’s National Toxicology Program put tungsten on its priority test list and is now pushing to determine whether the metal increases cancer rates in animals.

CDC’s data also highlight national concerns. Its first *National Report on Human Exposure to Environmental Chemicals*, released in 2001, revealed, for instance, that about 8% of all women of childbearing age—more than expected—have levels of mercury, a potent neurotoxin, higher than the level EPA generally regards as safe. The biomonitoring also showed that the average level in this group is four times higher than that in children—suggesting that regulators can’t extrapolate between the two groups. CDC is now measuring various kinds of mercury in people, to determine how much comes from fish, drinking water, or other sources. Researchers are also eager to see whether a revised Food and Drug Administration (FDA) advisory on fish consumption is making a difference.

What does it mean?

Biomonitoring doesn’t always clear the air, though. CDC tends to pick chemicals for which toxicity data indicate a human health effect. But it also chooses chemicals that are of potential concern because of animal studies that suggest a danger and the number of people of likely exposed. And when toxicity is not clear-cut, it becomes difficult to know what to make of the findings.

Take phthalates, chemicals found in a wide range of consumer products. In 2000, CDC published a paper on a subset of 289 adults from NHANES, the largest look at these chemicals at that time. Metabolites of several phthalates were higher in women aged 20 to 40 than in other groups. These are ingredients used in nail polish, cosmetics, and other personal-care products such as



Worry? EWG found, on average, 91 chemicals in people. For many, health effects are unknown.

A Snapshot of the U.S. Chemical Burden

Highlights from the Centers for Disease Control and Prevention’s (CDC’s) 2003 report:

Lead. Blood lead levels continue to fall; 2.2% of children ages 1 to 5 had blood lead levels above 10 micrograms per deciliter, the amount set by the CDC as an unacceptable health risk, down from 4.4% in the early 1990s.

Environmental tobacco smoke. Measured by cotinine—a metabolite of nicotine—blood levels of secondhand tobacco smoke were down 75% in adults over the 1990s, due to workplace and other restrictions on public smoking. Levels in children declined by 58% but are still twice as high as in adults—which points out that new efforts need to be made to reduce children’s exposure to secondhand smoke, says CDC’s James Pirkle.

DDT. Although DDT levels have continued to decline since the 1980s, the compound shows up in people born after 1973—the year DDT was banned. Clearly, DDT persists in the environment, and it may be coming into the country in imported food, says Pirkle. Blood levels of DDE, a metabolite of DDT, were three times higher in Mexican Americans than in other groups, raising the question of where they are being exposed—while growing up in or visiting Mexico, or while living in the United States?

Organophosphate pesticides. Urine levels of these pesticides, including the insecticides chlorpyrifos and diazinon, turned out to be higher in children than in adults, perhaps because their metabolism is different from adults’. Researchers are watching closely to see if the levels go down nationwide, now that the compound has been banned for household use.

—E.S.

soap and shampoo, particularly those with fragrances added. Some evidence from animals indicates that the compounds can be estrogenic and could lead to reproductive toxicity. "CDC and NHANES data ... made people sit up and pay attention to phthalates," says Gina Solomon of the University of California, San Francisco, and the Natural Resources Defense Council.

EWG launched a campaign to remove these compounds from cosmetics and last week petitioned FDA to put warning labels about phthalates and other chemicals on personal care products. But an industry group fired back that the statements of possible danger to fetuses were "alarmist," and it pointed out that the second national report of 2003 (see sidebar on p. 1893), which includes many

more people than the initial study, didn't find elevated levels among 20- and 30-year-old women. CDC cautions, however, that there aren't any guidelines yet on what levels might cause health effects.

Polybrominated diphenyl ethers (PBDEs) are another case in point. The European Union and California have banned the compounds, widely used as flame retardants, after researchers discovered that levels in breast milk had shot up—even though nobody knows for sure whether these compounds are toxic to humans. Levels are still rising in the United States (*Science*, 18 June, p. 1730). Last year, the main U.S. manufacturer voluntarily began to phase out two PBDEs, but EPA hasn't regulated any. CDC is now measuring PBDEs.

For EPA, the problem is that the pace of biomonitoring has eclipsed that of the basic epidemiology and toxicology needed to reveal whether a chemical causes harm. A big step forward, researchers say, would be the multi-agency National Children's Study (*Science*, 11 July 2003, p. 162), a \$2.7 billion health survey intended to follow 100,000 children as they grow up, monitoring levels of environmental chemicals and looking for any associations with disease. It's ready to start in late 2005 if it can get \$27 million in funding. Such a prospective study is needed to answer the questions raised by biomonitoring, says Landrigan, a project booster. But it could be years if not decades before those answers are in. "There's no easy way to fore-shorten that," Landrigan says. —ERIK STOKSTAD

Profile Michael Majerus

In Defense of Darwin and A Former Icon of Evolution

After a severe drubbing, the famous example of the peppered moth is getting refurbished

CAMBRIDGE, U.K.—Michael Majerus's fascination for "bugs," as he calls all insects, was ignited at the tender age of 4. His mother can recall the exact moment: It was late summer, and he caught his first butterfly—a red admiral resting on a white chrysanthemum—with his bare hands. From that point on, he was hooked. At night when other children were in bed, the young Majerus roamed the English countryside tending his moth traps. Now 50 and in his 25th year of teaching evolutionary genetics at the University of Cambridge, Majerus still runs his moth traps most nights.

Majerus's research has focused on sexual selection, sex-ratio manipulation, and the evolution of melanism (the darkening of body color) in various moths, butterflies, and ladybirds. But over the past few years, half of his working life has been occupied by one controversial species, the peppered moth, *Biston betularia*, and an infamous study that's been attacked by both evolutionary biologists and anti-evolutionists.

Through his research, Majerus found himself embroiled in the scientific debate over the evolutionary forces behind melanism in the peppered moth. Experiments by British lepidopterist Bernard Kettlewell in the 1950s claimed to show that bird predation, coupled with pollution, was responsible for a color shift in the moth population. But problems with Kettlewell's methodology led some scientists to doubt his

conclusions. Majerus was not the first to point out the flaws, but by doing so, he inadvertently set off a wave of anti-evolutionist attacks. While acknowledging that Kettlewell made mistakes, Majerus believes Kettlewell was right in his conclusions and has taken it upon himself to prove it.

As Majerus shows off some of the roughly 100,000 peppered moth pupae he'll



Easy prey? Critics challenged the view that the moth population grew darker because birds were more likely to see and devour light individuals.

rear for his latest experiment, it's clear that he's prepared to go to great lengths to make his case. Once the moths begin to emerge in May, Majerus begins a daily grind. He releases them at dusk and gets up at dawn to observe their fate: counting how many are

plucked from their resting places by birds, and how many survive to see another night. He will continue this routine into August, as he has done for the past three summers. All he needs, he reckons, is another 2 years' worth of data—a total of some 4000 moth observations—to settle the controversy over whether bird predation is the major selective force in favoring one color form of the peppered moth over another.

Small and unobtrusive, the peppered moth doesn't look like the star in an evolutionary drama. But the rise and fall of the almost-black melanic form (*carbonaria*) in tandem with changing pollution levels has become the most famous example of evolution in action. Through his pioneering experiments, Kettlewell claimed to have demonstrated that melanic peppered moths were more common in industrialized areas because they escaped the attention of predatory birds when resting against soot-blackened, lichen-free bark. Because more of the darker ones survived to produce the next generation, he argued, entire populations grew darker.

But doubts emerged over Kettlewell's methodology in recent decades as researchers failed to replicate some of his results. His predation experiments were chiefly criticized for their artificiality: He placed the moths on exposed parts of trees in broad daylight, when they don't normally fly, rather than allowing them to settle naturally; he released them in large numbers, thereby inflating moth densities and possibly creating a magnet for predatory birds; and he used a mixture of lab-reared and wild-caught moths without checking to see whether they behaved the same way. Majerus summarized these criticisms in a book on the evolution of melanism in 1998

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