MEETING SOCIETY OF TOXICOLOGY

Hazards of Particles, PCBs Focus of Philadelphia Meeting

Some 5300 toxicologists met in Philadelphia from 19 to 23 March for the 39th annual meeting of the Society of Toxicology. Among the highlights were a symposium on the health effects of breathing fine particles and a study finding that PCBs may suppress toddlers' immunity.

Soot's Health Effects Strengthened

In the early 1990s, Harvard researchers published startling evidence implicating soot—or more specifically, particulate matter (PM)—in 60,000 deaths a year in the United States. Carol Browner, administrator of the U.S. Environmental Protection Agency (EPA), took these and related findings to heart, proposing stringent new regulations to control fine soot in 1996. But critics in industry and the scientific community immediately blasted the EPA for imposing costly regs on the basis of what they said was shaky science. New results, some of which were reported at the toxicology meeting, now bolster the case against fine particulates.

Dirty business. Scientists are filling in the picture of how particulate pollution in cities such as Philadelphia exacerbates heart and respiratory illness.

Some of the work is in fact an offshoot of the original brouhaha. The EPA went ahead with the new regs in July 1997, building in an 8-year delay for implementing them. Congress reacted by launching a massive research effort on the health effects of PM, approving around $50 million of EPA's budget for the research over the past 3 years and mandating that the National Research Council (NRC) oversee the studies.

The earlier work was criticized partly because other air pollutants that rise along with PM—nitrogen oxide, for example—can exacerbate cardiopulmonary disease and thus they, rather than PM, may have caused the effects the Harvard researchers saw. Critics also complained that direct evidence of how breathing fine particles makes people sick was needed (*Science*, 25 July 1997, p. 466). At the symposium, Harvard epidemiologist Douglas Dockery, a key author of the original studies, addressed the first issue with new work that tightens the link between PM and worsened heart disease.

In one experiment, his group and Arden Pope at Brigham Young University in Provo equipped seven Utah retirees with heart monitors during periods when the researchers knew air pollution would rise as an idle local steel mill cranked into operation. As reported last November in the *American Heart Journal*, the researchers found that during the periods of high pollution, the subjects' heart rates became less variable—an indication that they were at increased risk of having heart attacks. In another study, published in the January issue of *Epidemiology*, Dockery's team found that heart arrhythmias in 100 men with implanted heart defibrillators increased along with daily particulate levels.

Results from the Health Effects Institute (HEI), an industry and EPA-supported nonprofit organization in Cambridge, Massachusetts, further dispel doubts about the 1990s findings. In one study, epidemiologists led by Johns Hopkins University's Jonathan Samet found a "robust" association between PM monitor readings and deaths and hospitalizations in 90 U.S. cities. In addition, a reanalysis by an HEI panel of the original Harvard data shows that the results hold up even after trying several different statistical approaches.

While these and other studies are firming up the epidemiologic case against PM, new animal research points to the metals, such as vanadium and nickel, that are found in PM as a prime source of its toxicity. At the meeting, EPA toxicologist Penn Watkinson reported that he and his colleagues had exposed rats with weakened cardiopulmonary systems to mixtures of the metals. The team found harmful changes in the rats' heart function and increased deaths. By contrast, rats exposed to volcanic ash, which contains essentially no metals, were little affected.

Despite the plethora of research now under way, a host of questions remain about how PM does its dirty work. The metal studies, for example, used doses much higher than city dwellers typically encounter, warns toxicologist Joe Mauderly of the Lovelace Respiratory Research Institute in Albuquerque, New Mexico, who is a member of the NRC panel overseeing PM research. Other compounds in PM such as organics also likely play a role in its toxicity, but little is known about their effects. With definitive answers still not in, expect another wave of controversy in 2002 when the agency next reviews the data on the health effects of PMs—a step it must take before implementing the more stringent PM standard in 2005.

Low-Level PCB Dangers

Without question, PCBs are nasty chemicals. These polychlorinated biphenyls, as they are properly known, accumulate in the food chain and cause a variety of ill effects in lab animals, from liver damage to cancer. For that reason, most developed countries banned the use of PCBs and many similar chemicals decades ago. Despite that, PCBs can still be found, often in minute levels, in the body fat of all people examined. New evidence presented at the meeting now suggests that even these low levels of PCBs may affect development in young children.

The work comes from Nynke Weisglas-Kuperus, a developmental pediatrician at Sophia Children's Hospital in Rotterdam, the Netherlands, and her colleagues. They found that PCBs and related chemicals called dioxins, passed by Dutch mothers to their babies during pregnancy and in breast milk, appeared to weaken the infants' immune systems. This in turn contributed to more infections in the first 3 1/2 years of life, Weisglas-Kuperus reported. "These are really subtle effects," says dioxin toxicologist Linda Birnbaum of the U.S. Environmental Protection Agency. But, she adds, if they translate into lots more childhood infections over a population, "that has an impact."

Previous work in both animals and humans had suggested that PCBs and dioxins, which are still produced as byproducts of

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incineration and industrial bleaching, suppress the immune system. For example, they've been blamed for spurring a 1988 virus outbreak that killed 20,000 European harbor seals feeding on PCB-tainted fish. And in Taiwan, a group of infants born to mothers who had accidentally consumed high doses of PCBs in 1979 had an elevated rate of infections.

To find whether health effects might also arise from the lower exposures more typically seen in developed countries, in 1990 Weisglas-Kuperus and colleagues began a long-term study of 207 mothers and infants living outside Rotterdam. Roughly half the mothers nursed their babies and the others fed them formula, which was not contaminated with PCBs.

When the infants were 18 months old, the researchers detected slight changes in the immune cells of some of them, particularly those who had been breast-fed, suggesting that their immune systems had been influenced by PCB exposure and might be less able to fight infections. These changes correlated with PCB and dioxin levels in blood from the babies' umbilical cords and in the mothers' blood and breast milk. At that time, however, those with greater immune changes didn't get sick more often than the other babies.

That changed when the researchers reexamined the children at age 3 1/2, when a typical child has had many infections. As before, they found that the toddlers whose mothers had more PCBs in their blood had higher levels of certain T cells. The researchers then looked at the current level of PCBs in the children's blood and their history of infections. After adjusting for confounding factors such as parental smoking, which tends to increase infection rates in children, and breast feeding, which, while exposing the babies to PCBs, is also well known to boost immunity, they found that children with high PCB exposures at age 3 1/2 were eight times more likely to have had chickenpox, and three times more likely to have had at least six ear infections than those with lower exposure.

The Weisglas-Kuperus team continues to monitor the children for neurological and other effects. But she says the immune suppression alone underscores the importance of strict regulations on the release of PCBs and dioxins. —JOCELYN KAISER

MEETING AMERICAN CHEMICAL SOCIETY

Chemists Unveil Molecular Wizardry in San Francisco

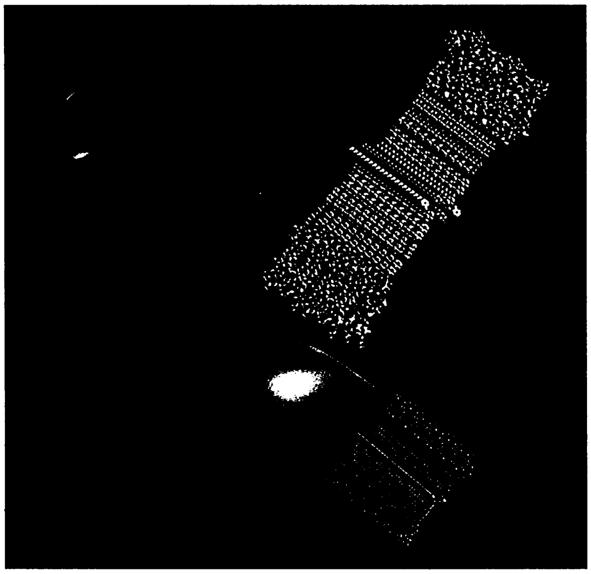
SAN FRANCISCO, CALIFORNIA—Baseball fans looking to check out the new stadium of the hometown Giants aren't the only ones flocking to the City by the Bay this spring. The 219th meeting of the American Chemical Society (ACS) drew nearly 20,000 chemists, physicists, biologists, and engineers from around the globe from 26 to 30 March. Among the meeting's home runs were reports of novel organic molecules that give old plastics new life and a new alternative to DNA chips.

Ribbons Make Tough Stuff

In fairy tales, a sprinkling of magic dust can make your dreams come true. In the world of plastics chemistry, that makes Samuel Stupp a wizard. At the ACS meeting, Stupp, a chemist at Northwestern University in Evanston, Illinois, reported developing new three-part molecules, a pinch of which can drastically change the strength and optical properties of commodity polymers such as those used to make coffee mugs and Plexiglas. Down the road, the new molecular seasoning could be used to lend everyday plastics like polystyrene the strength and toughness of a bulletproof vest at a fraction of the cost.

"It's really a unique approach" to polymer chemistry, says Timothy Long, a polymer chemist at Virginia Polytechnic Institute and State University in Blacksburg. "It's really remarkable how the properties [of the plastics] changed by adding so little of the new material."

Initially, Stupp and his colleagues weren't looking for a way to spice up tired plastics. Stupp's team had previously made two-part molecules called rodcoils, so named because half of each molecule was rigid, the other half flexible. And this unique structure, they found, caused the molecules to assemble into mushroom-shaped clumps that stacked themselves into sheets (*Science*, 18 April 1997, p. 354).



Cordon bleu. A dash of DRC molecules is enough to festoon a solvent with chemical ribbons that create a tough blue gel.

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For their current project, they wanted to see if they could tweak the chemistry of the rodcoils to coax them to form one-dimensional chains. They started by grafting a third section onto the rigid end of the molecules. This new portion, called a dendron, begins as a "Y" shaped group with two arms jutting from the end of the molecule. Each arm is capped by hydroxyl groups that can readily form weak hydrogen bonds with their neighbors. That gave them three-part molecules, which they dubbed "dendron-rodcoils," or DRCs. When the researchers dissolved a dash of DRCs in an organic solvent, they were surprised to find that the liquid solvent instantly turned into a gel. Evidently the DRCs were sticking together. Closer inspection showed that the DRCs had indeed lined themselves up, not into chains, but into ribbons.

When DRCs are added to a solvent, Stupp explains, the hydroxyl-tipped arms of one dendron meet up and form hydrogen bonds with hydroxyls on a second dendron, linking two DRCs together like pencils fused at their erasers. Afterward, the DRCs can still form additional hydrogen bonds, so as other molecular pairs drift by they line up alongside the first one. The result is a zipperlike structure only 10 nanometers wide but up to 500 nanometers long, with the hydroxyl "teeth" locked in the middle and the long bodies of the molecules trailing behind them. Still more hydrogen bonds in other parts of the molecules then link the ribbons into a web.

But the DRCs don't just force one another into line, Stupp says. The rib-