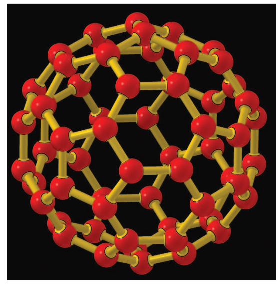
Fullerenes and Fish Brains

Nanomaterials Cause Oxidative Stress



As interest increases in the production and use of nanomaterials in consumer products such as sunscreens and cosmetics, pharmaceuticals, and industrial applications, so do concerns about human and environmental health effects as the tiny particles inevitably reach the soil, water, and air, and are eventually taken up by living organisms. Further direct human exposure will occur through workplace exposure during manufacture. Although there have been few studies to date on the potential toxicity of nanomaterials, research activity is growing. Now biologist Eva Oberdörster of the Duke University Marine Laboratory in Beaufort, North Carolina, and Southern Methodist University in Dallas, Texas, shows for the first time that one of the most popular nanomaterials, carbon-based particles known as fullerenes, can have adverse physiologic impacts on aquatic organisms [*EHP* **112:1058–1062**]. Oberdörster shows significant evidence of oxidative stress in the brains and gills of juvenile largemouth bass exposed for 48 hours to water laced with fullerenes at concentrations that may likely be found in the aquatic environment.

Nanomaterials are defined as manufactured substances where one dimension measures 1–100 nanometers. Within the last few years, large-scale industrial production of tons of fullerenes has begun for a diverse and growing range of commercial applications, including sunscreens, coatings for bowling balls, and fuel cell membranes. Previous research with ambient nano-scale particles such as ultrafine particulate matter has demonstrated that some of these particles tend to migrate into cell membranes and mitochondria, and that a selective pathway transports them into the brain in mammals. Oberdörster hypothesized that fullerenes might follow similar pathways, and that because they are reactive with oxygen and attracted to lipids—both of which are components of oxidative reactions—they could cause oxidative damage in the brains of fish.

Fullerenes are typically coated during the manufacturing process to reduce potential toxicity, and it is unknown how long the coating will persist when the molecules are exposed to the environment. However, cell culture experiments have suggested that the coating may break down quickly upon exposure to air or ultraviolet radiation. Therefore, Oberdörster used uncoated fullerenes in her tests, at concentrations of 0.5 and 1.0 parts per million, comparable to typical concentrations of other lipophilic chemicals currently found in the aquatic environment, such as polycyclic aromatic hydrocarbons.

Oberdörster found that lipid peroxidation, a sign of free radical oxidative damage, was significantly elevated in the brains of several of the fish, though there was no clear dose response. The lipid-rich character of the brain lends credence to the suspicion of a selective lipid pathway, although the mechanism is still undetermined. Lipid peroxidation actually decreased in the animals' gills and liver. However, there was evidence in the gills of a depletion of the antioxidant compound glutathione, indicating that those tissues also were undergoing oxidative stress.

Interestingly, Oberdörster also observed that the water in the fullerene tanks was clearer than that in control tanks. She speculates that this may have been due to interference by the fullerenes with the growth of beneficial bacteria normally found in aquaria. Although the phenomenon has not been documented, she suggests that this potential risk of damage to the microbial community would be an important subject for future research.

Oberdörster writes that the effects she found in fish could be predictive of similar effects in humans. With fullerenes and other nanomaterials likely to be used widely in the near future, she stresses that research efforts should be intensified in order to prevent the possibility of damage to human health and the environment. **–Ernie Hood**

Buckyballs and bass. Research shows that nanoparticles called fullerenes (or "buckyballs," after namesake R. Buckminster Fuller), upon making their way into the environment, can have adverse physiologic impacts on aquatic life.

Copper in Drinking Water

Using Symptoms of Exposure to Define Safety

For the past five years, a team at the University of Chile's Institute of Nutrition and Food Technology in Santiago, led by Magdalena Araya, has been assessing the response of healthy adults to varying concentrations of copper in drinking water. Their goal is to define safe limits for the early, acute effects of excessive copper exposure via drinking water. Their latest report verifies earlier findings that gastrointestinal symptoms such as nausea, abdominal pain, diarrhea, and vomiting occur when copper concentrations reach 4.0–6.0 milligrams per liter (mg/L) [*EHP* **112:1068–1073**]. This provides the best confirmation to date that the World Health Organization's (WHO) current drinking water limit for copper of 2.0 mg/L is reasonable.

Copper is an essential nutrient needed to prevent anemia and keep the skeletal, reproductive, and nervous systems healthy. The U.S. National Research Council currently recommends that adults receive 1.5–3.0 mg of copper daily to prevent deficiencies. However, the health effects of high copper intake are poorly understood.

Reports of copper poisoning are uncommon, and are linked to eating fruit sprayed with copper fungicides, cooking food in copper vessels, or ingesting grams of copper sulfate in suicide attempts. In such cases, copper toxicosis damages the liver and kidneys. The copper content of most of the world's natural water supplies does not exceed more than a few milligrams per liter, although concentrations can be higher in well water and in hard water delivered through newly installed copper pipes.

Araya and colleagues are working to identify markers of early biologically relevant effects of copper deficiency and excess. Past studies have shown that gastrointestinal symptoms are better indicators of acute exposure to copper than biochemical markers, such as blood copper, serum ceruloplasmin, and the activity of liver enzymes. According to Araya, copper absorption from food is unlikely to induce acute gastrointestinal responses, whereas the pH of water favors copper solubilization and absorption, which induce gastrointestinal effects. Therefore, it becomes important to define the copper concentrations in drinking water that cause gastrointestinal symptoms.

The current randomized, double-blind, community-based study monitored 1,365 people from 441 families. The subjects ranged in age from 18 to 60 years. For two months each family's drinking water was spiked with copper at concentrations of <0.01, 2.0, 4.0, or 6.0 mg/L. The lowest copper intake represented the concentration of copper in Santiago's tap water. The higher concentrations reflected the WHO guidelines (2.0 mg/L) and levels noted in earlier studies to produce nausea (4.0 mg/L) and vomiting (6.0 mg/L). Participants were told to switch to plain tap water for 48 hours if they experienced any of a list of symptoms. If symptoms recurred after participants resumed drinking the copper-treated water, they were told to permanently switch back to plain water. Each household kept a daily diary of water consumption and symptoms.

About 16% of the participants experienced at least one gastrointestinal symptom, with nausea and abdominal pain described most often. All dosage groups reported some symptoms, although the numbers in the two lowest-dosage groups were not statistically significant. Women reported two-thirds of the symptoms. They also appeared more sensitive to copper than men—for instance, during the first week, women's symptoms occurred at 4.0 mg/L, compared to 6.0 mg/L for men.

The team's latest results confirm the findings from their earlier studies, which involved controlled clinical trials with smaller numbers of people. According to the authors, given the lack of statistically significant effects in the lower-dosage groups, the results support the WHO guideline of 2.0 mg/L copper in drinking water as a safe limit. **–Carol Potera**

Lead in Mexican Children

Pottery Use Slows Reductions in Blood

Getting the lead out of Mexico City gasoline has contributed to a significant drop in the blood lead of local children, as it has elsewhere in the world, according to what is likely the first long-term study of such effects in a single group of people [*EHP* **112:1110–1115**]. But the drop within children wasn't nearly as large as the drop in the air might have suggested. Other lead sources such as ceramic pottery and local industry, combined with poor nutrition, likely are keeping blood lead concentrations elevated at levels 3–4 times higher than those found in U.S. children, concludes a team of researchers led by Lourdes Schnaas of the Mexican National Institute of Perinatology.

The team began its study by recruiting 502 pregnant women attending the institute's prenatal clinic in Mexico City. The researchers followed 321 healthy children born to these women between 1987 and 1992. Team members followed each child for 10 years, taking blood samples every six months. They also tracked airborne lead concentrations using government data.

The study period coincided with government actions that led to sharp drops in lead in gasoline, with total elimination by September 1997. Those moves helped slash mean yearly airborne lead concentrations from 2.8 micrograms per cubic meter ($\mu g/m^3$) in 1987 to 0.07 $\mu g/m^3$ in 2002.

The children's mean blood lead dropped concurrently. In the group of children born earliest in the study (while most gasoline was still heavily leaded), 89% exceeded the present Mexican action limit for child blood lead of 10 µg per deciliter (dL) at age 2, whereas in the latest-born group only 26% exceeded the limit. For the 100 children with complete data, the peak average of 10.5 µg/dL at age 2 dropped to 4.9 µg/dL at age 10. The children without complete data had somewhat higher concentrations, but saw a parallel drop.

Although significant, none of these drops were nearly as dramatic as the drop in airborne concentrations. The team speculates that poor nutrition—as indicated in other Mexico City studies showing low intake of key nutrients such as iron—may have contributed to higher blood lead in the children. Low intake of essential nutrients including iron, calcium, zinc, potassium, and copper has been shown in numerous studies to be associated with increased absorption of lead.

The team found that children living in residential and mixed-use sectors of the metropolitan area had blood lead concentrations about 11% and 7% lower, respectively, than children in the more industrial northeastern area. In addition, socioeconomic differences showed a strong influence. Children in the lowest socioeconomic group had blood lead concentrations 32% higher than the highest group.

The team also found that children in families that used lead-glazed ceramics had blood lead concentrations 18.5% higher than children in families that didn't. One-third to one-half of the children's families used lead-glazed pottery, depending on socioeconomic stratum, with the greatest use among poorer families. A strategy of educating parents about the tainted pottery during the course of this study did not help much; families still used the pottery on occasion, and children could use similar pottery at other family members' homes.

The problem of lead leaching from certain ceramic glazes has been recognized for more than a century, and in 1993 Mexican officials passed regulations cutting the lead content in pottery. But the businesses that make and sell such pottery are poorly monitored, and many are small family enterprises with no quality control. Today, lead-glazed pottery remains one of the greatest sources of lead exposure for Mexicans. Thus, conclude the researchers, eliminating tainted dishes and pots through better regulation of the ceramics industry is needed to further reduce lead body burden. **–Bob Weinhold**

No bowl of cherries. Locally made glazed pottery remains a significant source of lead exposure for Mexican children.