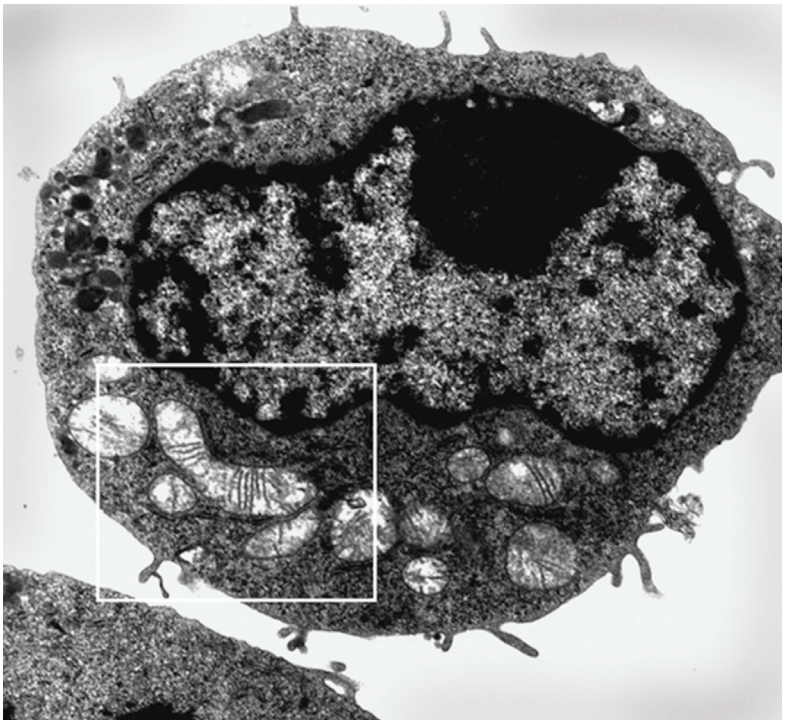
Cellular Energy Crisis

Particulate Hitchhikers Damage Mitochondria

One of the body's most important processes—energy production by mitochondria in the cell—can be significantly disrupted by exposure to ultrafine particulates, according to a team of researchers from the University of California, Los Angeles, and the University of Southern California [***EHP* 112:1347–1358**]. Furthermore, the researchers say, the primary culprits are substances that are attached to particles. These findings provide the first insights into the specific mechanism by which ultrafine particles, increasingly recognized as environmental villains, damage mitochondria, says principal investigator Andre Nel.

The researchers conducted a series of experiments that evaluated the effects on mouse liver mitochondria of either diesel exhaust particles (DEPs), ambient ultrafine particles collected in the Los Angeles area, or engineered nanoparticles with no attached chemicals. Using the DEPs and ultrafines collected in Los Angeles, the team isolated organic "hitchhiker" substances such as polycyclic aromatic hydrocarbons (PAHs) and quinones that had attached to the particle cores. These chemicals were tested for a variety of effects on cells and mitochondria.



Energy drains. New research conducted on mouse liver cells shows that toxicants that "hitchhike" on particulates severely interfere with the ability of mitochondria (framed, above) to produce energy.

Source: Li N, Sioutas C, Cho A, Schmitz D, Misra C, Sempf J, et al. Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage. Environ Health Perspect 111:455–460 (2003).

Among the adverse effects observed were mitochondrial structural decomposition, mitochondrial swelling due to increased membrane porosity and rupturing, increased production of free radicals, and induction of cellular death. Although some of these effects were dependent on the presence of calcium, others were caused by direct damage to the mitochondrial membrane.

The mitochondrial effects varied with the specific hitchhiker substances tested. For instance, polar fractions high in quinones were much more potent in inducing cell death, whereas aromatic compounds high in PAHs had a more moderate effect, and aliphatic compounds had no apparent effect.

Even within a class of compounds, not all substances proved to be equally destructive. For instance, among quinones, phenanthraquinone and 1,2-naphthoquinone caused mitochondrial swelling, while anthraquinone did not. This difference may depend on the ability of particular quinones to participate in reactions that generate reactive oxygen species (ROSs), unstable compounds that can quickly react with and damage other substances.

The team speculates on the biological mechanism behind the observed effects, laying the groundwork for future research. In the case of quinones, they suggest that the substances may redirect electron transfers in the inner mitochondrial membrane to molecular oxygen, thereby generating ROSs that can damage the mitochondria as well as exert proinflammatory effects. These effects could be important in the exacerbation of asthma.

Regardless of the specific mechanism, the consistent culprits in damaging mitochondria were the organic substances attached to particle cores. In contrast, engineered polystyrene nanoparticles with no organics attached had no apparent effects, leading the team to speculate that the small size of engineered nanoparticles may not be solely responsible for inducing mitochondrial and cellular damage. This is of considerable interest to the burgeoning field of nanotechnology, where there is concern that nanoparticles may be toxic based on small size alone.

The researchers acknowledge that smaller particles tend to penetrate better than larger particles and possibly are more bioavailable, due to their higher surface-to-volume ratio. These characteristics may allow organic chemicals that are attached to particle surfaces to better penetrate tissues than if they are not carried along by tiny transporters. **–Bob Weinhold**

Measuring by Hand

Arsenic Picked Up from the Playground

Several nations today ban or severely restrict the use of wood preserved with chromated copper arsenate (CCA), but many existing structures still remain—for example, about 70% of existing U.S. single-family homes and 14% of public playgrounds incorporate CCA-treated wood. In recent years, scientists have studied how arsenic leaches from CCA-treated wood, but they have only inferred exposure levels from measurements of arsenic concentrations in soil and sand near treated wood structures. In this issue, Elena Kwon of the University of Alberta and colleagues report on direct measurements they made of arsenic on the hands of children playing in playgrounds, some with CCA-treated wood structures and others without [***EHP* 112:1375–1380**]. The team reports that although playing on treated structures increases the amount of arsenic on children's hands, washing the children's hands after playing may be enough to avoid the health risks associated with CCA.

For several decades, CCA-treated wood was widely used in the United States, Canada, and other countries for playground equipment, fences, and backyard decks. Bans and restrictions on the use of CCA-treated wood have been driven largely by concerns that treated wood could release chromium and arsenic, posing risks to human health. Especially vexing was the possibility that children who contacted CCA-treated wood structures were, because of their propensity for hand-to-mouth contact, especially at risk for ingesting arsenic. Although touching treated wood will not liberate the 70- to

170-milligram dose of arsenic that is fatal to humans, ingesting lower doses of the substance has been linked to several cancers and other ailments.

The scientists measured arsenic on the hands of 130 children who visited 16 public playgrounds in Edmonton, Canada, over the period 5–21 August 2003. They tested all children who visited the playgrounds during randomized observation times and whose parents allowed them to participate in the study. The children averaged 4.75 years of age and spent an average of 1.25 hours on the playground.

When each child was finished playing, his or her hands were rinsed for 1 minute in a Ziploc bag of deionized water. The water and any soil/sand rinsed from the child's hands were analyzed separately in the laboratory for arsenic content. The team also collected soil/sand samples from each playground; samples from near the structures provided a measure of the arsenic that had leached from the wood, while those taken far from the structures indicated how much arsenic was present naturally.

In comparing playgrounds with and without CCA-treated wood structures, the team found no statistically significant difference in the amount of arsenic in the soil/sand samples or in the soil/sand washed from the children's hands. However, children who had played in the treated-wood environment had an average of 0.50 micrograms of soluble arsenic rinsed from their hands—more than five times as much as the children who did not play on treated structures.

Picked up on the playground. Arsenic from treated wood play structures is transferred to children's hands, but washing can remove most of it.

EPA research indicates that ingestion, rather than inhalation or dermal absorption, is the primary route of exposure related to arsenic-related ailments. Children aged 2–6 typically ingest about half of whatever they collect on their hands. But even assuming that the children in the study managed to ingest all of the arsenic on their hands, their average dosage was less than the average Canadian child's daily dose of arsenic through food and water (about 0.6 micrograms per kilogram body weight).

The scientists also found that the first rinsing removed most of the arsenic from the children's hands. That could be the prescription for parents whose children frequent playgrounds with treated-wood structures—and who want to play it safe. **–Scott Fields**