PM and Elevated Inflammation Markers

More Support for Air Pollution–Heart Disease Link

After evaluating about 1,000 Europeans already suffering from cardiovascular disease, researchers have found a relationship between elevated concentrations of airborne particulates (PM) and increases in two markers of inflammation that have strong links with cardiovascular diseases and deaths [***EHP* 115:1072–1080; Rückerl et al.**]. The cumulative number of people studied is the largest to date for PM and these inflammation indicators, with the findings generally consistent across diverse locales.

The researchers evaluated about 100 to 200 myocardial infarction survivors in each of six cities around the continent: Athens, Augsburg, Barcelona, Helsinki, Rome, and Stockholm. The cities have a wide range of demographic profiles, climates, and air pollutant concentrations. The selected people tended to be male, elderly, overweight, and consumers of numerous prescription drugs.

To evaluate inflammation, the researchers studied interleukin 6 (IL-6; thought to play a central role in triggering inflammation) and two proteins, fibrinogen and C-reactive protein (CRP), whose synthesis is stimulated by IL-6. They also considered the potentially confounding effects of many other variables, such as smoking status, presence of diabetes, time of day, and season.

They found that IL-6 increased most when particle number concentration—an indicator of ultrafine particulates—was elevated 12 to 17 hours before a blood draw. They also found that increased fibrinogen was associated with cumulative five-day exposure to larger particulates (PM_{10}). In addition, the results indicated associations between fine particulates ($PM_{2.5}$) and fibrinogen, and between nitrogen dioxide and IL-6.

There were a few anomalies that remain to be explained, such as the fact that the strongest link between PM_{10} exposures and increased fibrinogen after three days occurred in Helsinki, even though that city had the lowest PM_{10} concentrations of the six studied. There were no consistent patterns for CRP, although the results may have been skewed by the fact that most of the people studied consumed statins, cholesterol-lowering drugs known to reduce this protein.

Much remains unknown about the links between the inflammation indicators tracked and subsequent health effects. Nonetheless, this study may help explain conflicting results of similar work, since it better addresses previous limitations such as lack of geographic diversity, small subject population, limited number of inflammation indicators tested, and variable health status. **–Bob Weinhold**

Resisting Arrest

Drug-Resistant *Campylobacter* Persists in Poultry

Doctors use the fluoroquinolone class of antibiotics to treat food poisoning caused by *Campylobacter*. But after poultry farmers began using fluoroquinolones to treat respiratory disease in flocks, the drugs became less effective in people. In 2005, the FDA banned the use of fluoroquinolones on poultry farms because of these concerns. A new study now suggests that the ban may not be enough to fix the problem [***EHP* 115:1035–1039; Price et al.**].

Tony Campbell/Shutterstock

A team of Johns Hopkins researchers made weekly trips to Baltimore supermarkets for 20 weeks in 2004 and 15 weeks in 2006. Each week, they bought chicken from each of five different producers. Three producers had never used any antibiotics; two were major conventional producers that declared they had ceased all use of fluoroquinolones in 2002, three years before the FDA ban. The scientists tested one piece of chicken from each package for *Campylobacter*, confirmed the bacterium's identity using DNA analysis, then tested for antibiotic resistance using the minimal inhibitory concentration method.

The bacteria from conventional chicken were more likely to be fluoroquinolone-resistant than those from antibiotic-free products. The researchers compared each poultry producer to every other producer in a pair-wise fashion. In both 2004 and 2006, this statistical analysis showed that the *Campylobacter* strains from the conventionally produced chicken were more likely to be resistant than the strains from antibiotic-free samples.

In addition, between 2004 and 2006, the proportion of antibiotic-resistant bacteria on the conventionally produced chicken showed no significant change, indicating that the prevalence of fluoroquinolone-resistant *Campylobacter* was not decreasing in chicken from these producers, even after four years.

The results suggest that once antibiotic-resistant bacteria have developed, they may show up on grocery store shelves long after drug use stops. The authors note that they could not verify claims of voluntary fluoroquinolone prohibition because poultry producers are not required to report their use of drugs in food animals to regulatory agencies.

Other studies have shown that resistant bacteria can linger in poultry farms' water distribution and ventilation systems and in reused litter. The authors state that additional interventions, such as requiring thorough disinfection and regular litter changing in poultry houses, may be necessary to reduce the public health burden of fluoroquinolone-resistant *Campylobacter*. **–Angela Spivey**

Manganese and Infant Mortality

Well Water May Raise Death Rates in Bangladesh

Many wells in Bangladesh exceed the WHO threshold for manganese of 0.4 mg/L—in the Araihazar region in eastern Bangladesh, 80% of the wells provide water with manganese concentrations above 0.5 mg/L. A new study now suggests that manganese exposure through drinking water may contribute to Bangladesh's extremely high infant mortality rate of 54 per 1,000 live births [***EHP* 115:1107–1112; Hafeman et al.**].

Well water in Bangladesh already receives close scrutiny for its naturally high levels of arsenic, a known carcinogen. Manganese is also a concern, however, due to research showing associations between exposure and subclinical neurological effects in adults and decreased intellectual function in children. Additionally, neonatal animal studies have linked reduced weight gain and decreased survival to manganese exposure.

An ongoing cohort study in Araihazar, the Health Effects of Arsenic Longitudinal Study (HEALS), provided the framework for investigating whether manganese might affect human infant survival. Of the HEALS participants, 1,628 women met the criteria for the current study: they married before age 40, drank from the same well for most of their reproductive years, and reported at least one live birth. The researchers considered concentrations of manganese and other metals in the wells used by the target population, the mothers' reproductive history and education, and the families' socioeconomic status and other factors that can affect infant survival.

Although breastfeeding rates are high in Bangladesh, newborns are often given sugar water in place of colostrum, and most young infants receive complementary foods by age 6 months. Of the 3,824 infants born to the study group, nearly 85% were exposed to water manganese levels above 0.4 mg/L, and 335 died before age 1 year, an elevated risk of death not explained by measured covariates. The finding was more pronounced when restricted to women married after 1991, who appeared to give more complete reproductive histories; among these women, the infant death rate was 82 per 1,000 live births.

No dose–response relationship was seen, though, and the association was not found when analysis was restricted to water samples collected for the current study. The researchers recommend designing a study specifically to investigate the role of manganese exposure in infant mortality, with particular attention to causes of mortality and potential routes of exposure. **–Julia R. Barrett**

Mother and newborn in Dhaka, Bangladesh

Dieter Telemans/Panos Pictures

New Phthalate Link?

DEHP Metabolites and Altered Thyroid Hormone Levels in Men

Human studies have shown widespread exposure to phthalates, compounds used in the manufacture of household, consumer, and medical products. The plasticizer DEHP is one of the most widely used chemicals in this class. A limited number of rat studies have linked DEHP exposure to alterations in thyroid signaling and lower plasma thyroxine (T_4) concentrations. Now a study of adult men for the first time shows an association between higher urinary levels of the metabolite MEHP and reduced thyroid hormone in blood serum [***EHP* 115:1029–1034; Meeker et al.**].

Phthalates are metabolized and excreted quickly; these metabolites, rather than the parent diesters, are believed to be the active toxicants. Ingested DEHP is initially hydrolyzed in the intestine to MEHP. The metabolites MEOHP and MEHHP are then produced by the oxidation of MEHP.

The study participants included 408 men between the ages of 18 and 55. All were partners in subfertile couples who visited a Boston fertility center between January 2000 and May 2004. Each man completed a questionnaire and provided urine and blood samples on the same day. Blood samples were analyzed for free T_4, total triiodothyronine (T_3), and thyroid-stimulating hormone. Urine analysis provided data on concentrations of DEHP metabolites.

MEHP was detected in 83% of the 408 samples. MEOHP and MEHHP were found in more than 95% of 208 samples tested (the sample size was smaller because methods for analyzing these metabolites became available only later in the study).

Multivariate regression analysis revealed a statistically significant inverse association between urine MEHP concentrations and serum total T_3 levels. In an effort to determine whether individual differences in the ability to further metabolize and neutralize MEHP might explain this relationship, the researchers also calculated the percentage of MEHP relative to the other metabolites. They found a weaker though still statistically significant inverse association between the percentage of MEHP relative to the other metabolites and free T_4 levels.

This suggests that an individual's ability to metabolize and neutralize MEHP may play a role in determining effects. The researchers urge other scientists to consider whether MEHP levels relative to other metabolite concentrations might serve as potential markers for metabolic vulnerability to adverse effects from DEHP exposure. **–Rebecca Renner**