Asthma in Young Children

Prenatal DDE Exposure May Increase Risk

Most countries have banned the agricultural use of the organochlorine insecticide DDT because of the way this persistent, fat-soluble compound accumulates in the food chain. However, DDT is still widely sprayed in developing countries to combat malaria-bearing mosquitoes. Studies have linked exposure to DDT and its persistent metabolite *p,p′*-DDE to changes in the immune responses of human cells, and to asthma prevalence in children and adults. A longitudinal study now shows that prenatal exposure may provide the fundamental window for asthma susceptibility linked to DDT [***EHP* 113:1787–1790**].

Investigators collected umbilical cord blood from 482 children born on the Spanish island of Menorca and tested 84% for the presence of organochlorine compounds. DDT is not used on Menorca. However, the parents of the children in the study ate relatively large amounts of fish, which can be a source of exposure to DDT residues. According to self-reports of diet on questionnaires, more than half of the mothers ate fish more than twice a week during pregnancy.

All of the children tested had *p,p′*-DDE in their cord serum (the median concentration was 1.03 nanograms per milliliter [ng/mL]). Serum levels tended to be higher in children with older mothers, although the mothers' fish consumption during pregnancy correlated poorly with the children's DDE levels. Each child's serum also contained hexachlorobenzene and polychlorinated biphenyls.

Then and now. A study of Spanish mother–child pairs shows that DDT exposure *in utero* may contribute to later asthma in children.

The researchers correlated the children's prenatal exposure to risk of having asthma or atopy at age 4. Asthma was defined as one or more episodes of wheezing in the fourth year alone, one or more episodes of wheezing per year in consecutive years ("persistent wheezing"), or a physician's diagnosis of asthma. Atopy was defined as having blood levels of specific immunoglobulin E antibodies for dust mites, cats, or grasses. Of the initial participants, 97% provided medical information yearly through age 4 and 75% provided blood samples at age 4; 306 of these samples were tested for antibodies and for peripheral white blood cells, a sign of the underlying inflammation responsible for asthma.

Wheezing was reported at age 4 for 11.6% of the children whose blood was tested for organochlorines. In addition, 12.6% of those who gave blood at age 4 had antibodies for the specified allergens in their blood. The risk of wheezing increased with the concentration of *p,p′*-DDE in the child's cord serum. Of the children in the lowest quartile of exposure (less than 0.57 ng/mL), 9% reported wheezing compared to 19% of the children in the highest quartile of exposure (more than 1.90 ng/mL). There were no correlations between wheezing in the children and maternal consumption of fish during pregnancy.

There was no apparent link between atopy and the relationship between DDT and wheezing; children both with and without atopy had a similar increase of wheeze with increasing *p,p′*-DDE. The researchers speculate that the lack of an association between DDT exposure and atopy in their study could be due to the young age of the children studied, as sensitization to allergens tends to increase during childhood. There was no correlation between the other organochlorine compounds measured and wheezing or atopy.

Further study is needed to determine if the link between DDT and asthma susceptibility is caused by the effect of the insecticide on the immune system or the hormonal system. In addition to its direct impact on immune cells as shown in previous research, *p,p′*-DDE has also been shown to interfere with hormonal receptors and to mimic estrogen activity, which might indirectly affect immune responses. The researchers suggest that their results be considered when evaluating the risk of spraying DDT in anti-malaria campaigns. **–Kris Freeman**

Death by Particles

The Link Between Air Pollution and Fatal Coronary Heart Disease in Women

A growing body of evidence links chronic exposure to air pollution—especially particulate matter (PM)—with mortality resulting from a variety of heart, lung, and respiratory diseases. A new study corroborates this association, and indicates that women may be at greater risk than men of fatal coronary heart disease (CHD) as a result of exposure to airborne PM [***EHP* 113:1723–1729**]. When ozone (O_3) or sulfur dioxide (SO_2) is also present, women's risk appears even greater.

The study, by a team of epidemiologists at Loma Linda University, is part of the 22-year Adventist Health Study on the Health Effects of Smog. It followed 3,239 nonsmoking, non-Hispanic white adults in several mainly urban areas in California from 1976 to 1998. The researchers associated CHD deaths with prior exposure to various levels of several common

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air pollutants: $PM_{2.5}$, $PM_{10–2.5}$, PM_{10}, O_3, SO_2, and nitrogen dioxide (NO_2).

Participants completed a baseline health and lifestyle questionnaire in 1976, and four subsequent questionnaires covering personal sources of air pollution, such as secondhand tobacco smoke and fumes in the workplace. The researchers used airport visibility measurements (for $PM_{2.5}$ only) and data from state-run air pollution monitors (for all other pollutants) to estimate pollutant levels over time for the zip code centroids of participants' work sites and residences. Documented pollutant levels ranged from negligible to above legal limits. California's death certificate files and the National Death Index provided data on numbers and causes of deaths.

The researchers found that CHD caused 23.7% of all the deaths in the study cohort (155 women and 95 men). Adjusting for past smoking, body mass index, education level, frequency of eating meat, and calendar year (as PM levels declined over the study period), the researchers conducted statistical analyses to determine whether fatal CHD was associated with long-term exposure to the pollutants, either singly or in combinations of single gases and PM.

Women showed a relative risk for fatal CHD of 1.42, 1.38, and 1.22 with each increase of 10 micrograms per cubic meter ($\mu g/m^3$) of airborne $PM_{2.5}$, $PM_{10–2.5}$, and PM_{10}, respectively, in the air pollution they encountered during the four years preceding death. Postmenopausal women showed higher relative risks of 1.49, 1.61, and 1.30 for each 10 $\mu g/m^3$ increase in $PM_{2.5}$, $PM_{10–2.5}$, and PM_{10}, respectively. Neither O_3, SO_2, nor NO_2 was associated with fatal CHD on its own. O_3 and to a lesser degree SO_2 (but not NO_2) increased the effect of all sizes of PM. O_3 in conjunction with $PM_{2.5}$ yielded the most striking results: a relative risk of 2.0 in all women. Contrary to findings from several other studies that found increased risk of cardiopulmonary deaths due to PM in both genders, men showed no response to any of the pollutants.

The researchers highlight several physiological mechanisms that may explain their findings. Short-term exposure to PM is known to increase arrhythmia, inflammation, and blood viscosity, and to decrease heart rate variability, among other adverse effects that could lead to fatal CHD. Other findings show that O_3 exposure increases lung permeability, perhaps easing PM's entry into the bloodstream. Finally, several studies have indicated that PM deposits differently—and perhaps more harmfully—in women's lungs than in men's. This may provide a starting point for teasing out the study's finding of an association between PM and risk of fatal CHD in women, but not in men. **–Rebecca Kessler**

Tiny killer. Chronic low-level exposure to aflatoxins produced by *Aspergillus* molds (such as *A. flavus*, above) is associated with increased risk of liver cancer.

Liver Cancer and Aflatoxin

New Information from the Kenyan Outbreak

Millions of people are exposed to aflatoxins, toxic compounds produced by *Aspergillus* molds. These molds infest staple crops such as maize, peanuts, rice, and wheat throughout the world. Outbreaks of aflatoxicosis affecting up to several hundred people at a time have occurred sporadically, most recently in eastern Kenya in early 2004. An investigation of the Kenyan outbreak now yields new information on the risk factors associated with acute aflatoxin poisoning [***EHP* 113:1779–1783**].

Chronic low-level exposure to aflatoxins, particularly aflatoxin B_1, is associated with increased risk of developing liver cancer, impaired immune function, and malnutrition. Acute high-level exposure, which is less common, causes early symptoms of diminished appetite, malaise, and low fever. Later symptoms, including vomiting, abdominal pain, and hepatitis, signal potentially fatal liver failure.

The Kenyan outbreak followed a poor harvest of maize that had been damaged and made susceptible to mold by drought. Furthermore, to guard against theft of the meager harvest, people stored the maize in their homes, which were warmer and moister than the granaries where it was usually stored. From January to June 2004, 317 people sought hospital treatment for symptoms of liver failure, and 125 died. Health officials ruled out viral liver diseases; suspecting acute aflatoxin poisoning, they examined maize samples and found aflatoxin B_1 concentrations as high as 4,400 parts per billion (ppb), 220 times the Kenyan limit for food.

Researchers conducted a case–control study using records for 40 patients (cases) who had been hospitalized with acute jaundice during late May and early June and 80 randomly selected controls. Jaundice is a nonspecific symptom of liver damage.

Dennis Kunkel Microscopy

Participants or family members completed questionnaires targeting maize quality, storage, preparation, and consumption. The researchers collected 1-kilogram samples of maize from households that still had grain left over from the time of the outbreak for measurement of aflatoxin concentrations. Blood samples from 29 patients and 62 controls were analyzed for concentrations of aflatoxin B_1–lysine albumin adduct, a marker of aflatoxin exposure. The researchers also tested blood from 18 patients and 54 controls for hepatitis B surface antigen, an indicator of hepatitis B infection. In people with chronic low-level aflatoxin exposure, this virus enhances the risk of developing liver cancer.

Maize from patients' homes contained significantly higher amounts of aflatoxin (with a geometric mean of 354.5 ppb) compared to control households (with a geometric mean of 44.1 ppb). Patients' serum aflatoxin adduct concentrations, which were comparable to those measured in previous outbreaks, were nearly 10 times higher than those of controls. Further, patients who died had higher blood levels of adducts than those who survived. Forty-four percent of the patients tested positive for hepatitis B, compared to 7% of controls.

These analyses, with their greater level of detail, are the first to quantify the association between concentrations of aflatoxin in food, exposure history, concentrations of serum aflatoxin adducts, and acute aflatoxin poisoning. This study is also the first to quantify the independent association between hepatitis B infection and the effects of acute aflatoxin poisoning. The researchers suggest that monitoring both aflatoxin concentrations in crops and the incidence of acute jaundice could permit earlier recognition of food contamination and help prevent an outbreak from becoming widespread. Further, they suggest that future use of blood tests for aflatoxin B_1–lysine albumin adducts could serve to diagnose aflatoxin poisoning and to gauge the success of measures for reducing aflatoxin exposure. **–Julia R. Barrett**

Double jeopardy. Ergonomic stress may heighten the threat posed by on-the-job lead exposure.

The Heavy Load of Lead

Ergonomic Stress Heightens Exposure-Related Neuropathy

Long-term lead exposure among industrial workers can result in neuropathy (a disorder of the peripheral nervous system), while lower exposure levels cause muscle weakness. Until recently, however, the interaction between lead toxicity and chronic repetitive muscle use had not been investigated. Researchers from the Center for Occupational and Environmental Neurology in Baltimore now report that the impact of chronic lead exposure is augmented by concomitant ergonomic stress [***EHP* 113:1730–1734**].

The study included 80 lead smelter workers who were routinely exposed on the job to inorganic lead dust and (to a lesser extent) lead fumes. Historical blood lead records for all the workers were available from the smelter, which checked all employees' blood lead at least quarterly. These records showed that workers had high chronic exposure in the distant past, much lower exposure in the more proximate past, and still lower exposure at the time of the study. The researchers also measured current blood and bone lead levels and used the historical records to calculate two metrics of cumulative lead exposure—working-lifetime integrated blood lead (IBL) and working-lifetime weighted-average blood lead (TWA).

The team used the current perception threshold test to examine nerve fiber populations in the workers' shoulders, arms, wrists, and hands. This test measures the amount of electrical current needed to induce a sensation. The team also created a three-tiered ergonomic stress rating based on all the different jobs the workers had ever performed, cumulated over their employment history. This was used to arrive at a time-weighted average ergonomic stressor. Sensory nerve conduction threshold was measured in large myelinated, small myelinated, and unmyelinated nerve fibers.

The results showed that decrements in nerve function—a precursor to neuropathy—were limited to large and small myelinated sensory nerve fibers, with a threshold effect at a TWA of 28 micrograms per deciliter. At higher levels of lead exposure and presence of ergonomic stress, nerve fibers were more susceptible to increased damage, something that has never before been shown in human studies. The investigators suggest that nerves affected by lead are more susceptible to traction or mechanical compression, as would occur in the carpal tunnel of workers who perform activities such as heavy lifting and shoveling.

Measures of chronic lead exposure may serve as strong predictors of impaired nerve function. In addition, the authors believe they have been able to separate the impact of two components of cumulative blood lead—duration and intensity—with exposure intensity appearing to have a greater influence than duration on the outcome studied. Finally, the authors point out that although TWA and IBL are associated with peripheral nerve damage, bone lead—another measure of chronic exposure—is a weak predictor of lead effects in the nervous system because it reflects only that lead stored in the bone compartment and not necessarily the cumulative blood lead to which peripheral nerves were exposed. **–Dinesh C. Sharma**

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