

Particulate Soup

Identifying the Most Toxic Constituents of PM_{2.5}

Chronic exposure to air pollution has long been linked with cardiopulmonary-related mortality, and ambient fine particulate matter (PM_{2.5}) is often considered a primary cause of this association. Once inhaled, these particles can cause inflammation and oxidative stress. This in turn may result in systemic effects, including the buildup of

PM_{2.5} contributes to the haze that blankets metropolitan areas.



plaque deposits that can lead to heart attacks and strokes. A new study comparing air pollution exposure with health data gathered over a 5-year span now takes a closer look at which individual constituents of PM_{2.5} may be most likely responsible for associations between ambient air quality and mortality [*EHP* 118:363–369; *Ostro et al.*].

Ambient PM_{2.5} contains solid and liquid particles from many sources, particularly from fossil fuel combustion; among other constituents, it contains elemental and organic carbon, sulfates, nitrates,

iron, potassium, silicon, and zinc. The National Research Council has highlighted the importance of routinely collecting toxicity data on particle constituents to help refine air quality standards, target control strategies, and enhance the accuracy of health impact assessments.

In the current study, the authors used data from the California Teachers Study for 45,000 active and former female public school professionals. The teachers lived within 8 or 30 km of monitors that collected data on PM_{2.5} between June 2002 and July 2007. The large amount of individual-level data provided by participants allowed researchers to control for risk factors that could possibly confound the analysis. Smoking rates and indoor occupational exposures, for example, were very low in this study cohort, making it easier to identify an independent effect of outdoor air pollution. Air pollution measurements were generally taken twice a week, and information from health questionnaires also helped determine individual exposure.

Of 8 constituents studied, organic carbon and sulfates were found to be most strongly associated with all-cause, cardiopulmonary, ischemic heart disease, and pulmonary mortality. Even modest concentrations of these 2 constituents were associated with mortality from all 4 causes. According to the authors, the study provides new information to help focus and streamline regulatory efforts on a variety of sources of PM_{2.5}, including gasoline and diesel fuel, and other combustion activities. They write that the reduction of ambient PM_{2.5}, particularly from fuel combustion, may offer significant public health benefits.

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Endocrine Damper?

Flame Retardants Linked to Male Hormone, Sperm Count Changes

Additive flame retardants such as tris(1,3-dichloro-2-propyl) phosphate (TDCPP) and triphenyl phosphate (TPP), which are not chemically bonded to the products they are intended to protect, may escape into indoor environments such as homes, offices, and car interiors. A new study shows that men living in homes with higher amounts of TDCPP and TPP in their house dust had reduced sperm counts and altered levels of hormones related to fertility and thyroid function [*EHP* 118:318–323; *Meeker and Stapleton*]. Because the research to date suggests both compounds are ubiquitous in U.S. homes, the study points to a pressing need for further investigation into the sources and levels of day-to-day exposure to the compounds as well as their potential health effects.

TDCPP has long been the main flame retardant used in automotive foam cushioning, while TPP has been used for decades in a wide variety of applications, including furniture foam. Since polybrominated diphenyl ether (PBDE) flame retardants were banned in Europe and discontinued in the United States in 2004, the use of alternative flame retardants such as TDCPP and TPP has been on the rise. Indoor dust is known to be an important source of exposure to PBDEs (which also are additive compounds), and the authors suspect this could also be true for other flame retardants.

In the current study, TDCPP was found in 96% and TPP in 98% of the house dust samples. As has been reported for other flame retardants found in house dust, the concentrations of the flame retardants in the samples varied markedly, with ranges of <107–56,090 ng/g

for TDCPP and <173–1,798,100 ng/g for TPP. The concentrations of TDCPP in the men's homes were comparable to those of PBDEs, whereas the levels of TPP were considerably higher.

Because the study participants were part of a larger project involving men recruited from a Boston infertility clinic, the authors had access to information about the men's reproductive and thyroid hormone levels as well as their semen quality. They estimated associations for an interquartile range (IQR) increase in the level of each chemical measured in the dust samples, adjusting for potential confounders such as age and body mass. IQR analyses reflect the difference between the concentrations at the highest and lowest ends of the middle 50% of exposures.

This analysis revealed that each IQR TPP increase in the homes was associated with a 19% decrease in sperm concentrations and a 10% increase in prolactin levels. Increased prolactin can be a marker of decreased dopamine activity and also may be associated with erectile dysfunction. The authors also found that each IQR increase in TDCPP in the homes was associated with a 17% increase in prolactin and a 3% decline in free levels of the thyroid hormone thyroxine.

The findings mirror the limited toxicology data available on the study's end points. They are also consistent with findings on other organophosphate compounds such as the urinary metabolite of the insecticide chlorpyrifos [*EHP* 112:1665–1670; *Meeker et al.*]. The authors hope to follow up by exploring human exposure pathways for these flame retardant chemicals and by reassessing these relationships with markers of endocrine function among a greater number of men from the larger ongoing study.

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From One Womb to Another Early Estrogenic Exposures and Later Fibroid Risk

Uterine fibroids (leiomyomata) are the most common pelvic tumors in U.S. women as well as the most common cause for hysterectomy. Both estrogen and progesterone influence fibroid development, whereas early-life hormonal exposures can affect uterine development and a woman's response to estrogen or progesterone later in life. In a new study, researchers investigate novel hypotheses regarding fibroid pathogenesis in relation to early-life exposures, most of which have not been explored previously [*EHP* 118:375–381; D'Aloisio et al.].

The authors sought to determine whether *in utero*, early-life, and childhood exposures were linked with self-reported early fibroid diagnosis (by age 35) among non-Hispanic white participants in the NIEHS Sister Study. Participants completed self-administered questionnaires to assess intrauterine and early-life exposures. They also provided information on known and suspected risk factors for breast cancer and other end points including fibroids. The retrospective analysis included nearly 20,000 women who were 35–59 years old when they enrolled in the Sister Study.

The results showed an association between early fibroid diagnosis and having been fed soy formula during infancy, having a mother with pre-pregnancy diabetes, being born at least 1 month early, and low socioeconomic status during childhood. Early fibroid diagnosis also showed associations with prenatal exposure to diethylstilbestrol and with having a mother with gestational diabetes, although these associations were observed only among women who reported probable (versus definite) exposures.

The possibility of long-term health effects of soy formula is of interest because soy contains estrogenic isoflavones, and infants fed only soy formula consume more isoflavones (mostly genistein) per unit body weight than do adults who consume soy foods. The authors report a 25% increase in early fibroid diagnoses for women who had been fed soy formula compared with those who had not. Although the authors postulated the first 2 months of life may include a period more sensitive to isoflavone exposure, they were unable to demonstrate an association with soy formula intake during this time period specifically.

In rodent studies, neonatal treatment with genistein has been associated with later development of uterine cancer, abnormal mammary gland development, differences in hormone receptor levels in mammary glands, altered estrous cycles, reduced fertility, and early reproductive senescence (comparable to menopause in humans). However, there is a lack of human research in this area except for 1 study in which women who had received soy formula as infants reported increased menstrual pain and longer menstrual bleeding (which are symptoms of uterine fibroids).

This also was the first study to evaluate whether *in utero* exposure to maternal diabetes is associated with fibroids. Women whose mothers had diabetes before their pregnancy were twice as likely to report an early fibroid diagnosis as women whose mothers were not diabetic. The authors speculate that *in utero* exposure to maternal diabetes could alter methylation patterns in regions that affect expression of genes relevant to fibroid development.

The main strength of this study is its generation of novel and biologically plausible hypotheses for exploration in future studies. However, because this is the first epidemiologic study to evaluate most of these exposures, replication of findings in other populations is needed.

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Formaldehyde Exposure among Children A Potential Building Block of Asthma

Formaldehyde, a staple chemical in the manufacturing industry, is known to trigger acute adverse health effects such as skin, eye, nose, and throat irritation. Research on the human health effects of this compound has focused on a possible link between formaldehyde exposure and nasopharyngeal cancer. A new study reports the results of a meta-analysis of the literature examining a potential link between formaldehyde exposure and the prevalence of asthma in children [*EHP* 118:313–317; McGwin et al.].

Formaldehyde resins are used in the manufacture of furniture, clothing, carpeting, and pressed-wood products such as particle board and hardwood plywood paneling. The result is chronic human exposure to formaldehyde in many homes. The authors were inspired in part by concerns about formaldehyde exposure among displaced Gulf Coast residents living in temporary trailer housing after Hurricane Katrina.

The investigators analyzed data from 7 research articles concerning 5,930 total participants (364 with

diagnosed asthma) that included actual formaldehyde measurements. Results of a fixed-effect model—meaning the model did not account for variation among the 7 studies—indicated the prevalence of asthma was 3% higher with each 10- $\mu\text{g}/\text{m}^3$ unit increase in formaldehyde. A random-effects model—which did account for variation among studies—indicated a 17% increase in asthma with the same unit increase in exposure. When 1 unusually influential study was excluded from the meta-analysis, the authors estimated a 24% relative increase in asthma based on both fixed- and random-effects models. In addition, studies that measured formaldehyde exposure in schools suggested stronger associations than studies that examined home exposures.

The authors describe several limitations to the study, including the use of self-reported asthma information in some studies and the use of cross-sectional study design, which limits the ability of a study to tease out whether exposures preceded the development of asthma. Despite these limitations, the authors believe their results support a positive association between increased formaldehyde exposure and risk of childhood asthma. They note that future research regarding this health issue should focus on well-designed prospective epidemiologic studies.

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Formaldehyde is emitted by many manufactured wood products, which can contribute to high indoor exposures.

