Arsenic and Infectious Disease
A Potential Factor in Morbidity among Bangladeshi Children

Lower respiratory tract infection (LRTI) and diarrhea are two of the most common causes of morbidity and mortality in children under 5 years old, especially in low-income countries. A new prospective cohort study of the link between these types of infections and arsenic exposure revealed a dose-dependent increase in LRTI and diarrhea in relation to maternal arsenic exposure [EHP 119(5):719–724; Rahman et al.].

Earlier studies linked prenatal arsenic exposure to increased risk of infant mortality, and infectious disease has been suggested as a potential underlying cause in these deaths. No epidemiologic studies have been conducted to support that explanation, but there is evidence from a few animal and human studies that arsenic may cause immunosuppression.

The current study included 1,552 live-born infants of women enrolled during 2002–2004 in Matlab, Bangladesh. Arsenic exposure was assessed by measuring inorganic arsenic in maternal urine samples collected at gestational weeks 8 and 30. After birth, information on symptoms of LRTI and diarrhea in infants was collected at monthly home visits in which mothers recalled symptoms that had occurred over the previous 7 days.

Epigenetic Liver Damage
Study Reveals Clues Implicating 1,3-Butadiene

The petroleum-derived substance 1,3-butadiene is a known human carcinogen that is a significant contributor to cancer risk in the United States. There is evidence it causes liver, heart, lung, and hematopoietic cancers in rodents through genetic damage. But some researchers suspect it also may induce changes through other pathways, including epigenetic alterations, which occur when the function of a gene is altered while its DNA sequence remains stable. A new study provides further evidence 1,3-butadiene may indeed cause epigenetic damage [EHP 119(5):635–640; Koturbash et al.].

The authors exposed male C57BL/6 mice to inhaled 1,3-butadiene at two doses, 6.25 ppm and 62.5 ppm, for 2 weeks (6 hours per day, 5 days per week). The low dose is about 10–100 times higher than typical occupational and ambient exposures, respectively, while the inhalation pathway is considered the most common for human exposure. In the 5 mice exposed at each dose, the researchers found numerous dose-dependent alterations in genes linked with liver function. Compared with controls, mice in the low-dose group had 1 gene with a more than 2-fold increase in expression and 5 with a more than 2-fold decrease in expression. Mice in the high-dose group had 4 genes with a more than 2-fold increase in expression and 13 with a more than 2-fold decrease in expression. The high-dose mice also had a small but significant decrease in body weight.

The estimated relative risk of LRTI and severe LRTI increased by 69% and 54%, respectively, in the participants whose mothers had urinary arsenic concentrations in the highest quintile (262–977 μg/L), compared with offspring of mothers whose exposure was in the lowest quintile (less than 39 μg/L). The relative risk of diarrhea increased 20% for the highest-exposure group compared with the lowest-exposure group.

The authors observed that relative risks of LRTI and diarrhea increased irrespective of sociodemographic factors or nutritional status of the women. However, further evaluation is needed in a larger sample to evaluate possible effect modification, because the risks appeared more pronounced in low social strata.

Strengths of the study include the large sample size, the objective measure of arsenic exposure, and the followup of infants for one full year, which the authors say would reduce any influence of seasons on infection rates. Potential limitations include lack of measurements of infant exposure to arsenic, a lack of information about other potentially toxic substances in water and food, and reliance on mothers’ reports of disease symptoms and signs. Given the millions of people worldwide who drink well water with elevated arsenic concentrations, the study results could have serious public health implications and, taken together with previous studies showing health effects from this exposure, emphasize the need to reduce arsenic exposure via drinking water.

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The authors also found evidence of epigenetic changes that were consistent with altered gene expression in the liver. Changes in the attachment of methyl groups to DNA are a useful marker of epigenetic changes, and the researchers observed significant decreases in 5 markers of methylation in the high-dose group and smaller decreases in 4 of the 5 markers in the low-dose group. High-dose mice also had a roughly 50% decrease in another methylation indicator.

Changes in histones, proteins that help regulate gene expression, also occurred in the high-dose mice, with significant decreases in methylation based on 3 biomarkers. Expression of proteins involved in DNA methylation and histone methylation decreased while expression of a protein involved in histone demethylation increased, consistent with the observed decreases in DNA and histone methylation.

These findings fit with earlier research into epigenetic effects of other substances and are consistent with other mechanistic evidence of how such damage can play a role in the onset of various adverse health effects, the authors say. If additional studies—including studies of female mice, other mouse strains, and other animals—repeat these findings, this would indicate multiple modes of carcinogenicity for 1,3-butadiene and could lead to establishment of specific biomarkers for epigenetic damage that could be used in future toxicity and exposure assessments.

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