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RESEARCH BRIEF 121

Impacts of Low-Level Benzene Exposure

Benzene is a ubiquitous environmental contaminant. It has been found at over half of the National Priorities List sites identified by the Environmental Protection Agency, and we are all routinely exposed to benzene via second-hand cigarette smoke, automobile emissions and gasoline vapors. Benzene is one of the most frequently used chemicals in American industry as it is used as a solvent and to make plastics, resins, adhesives, synthetic fibers, lubricants, dyes, detergents, drugs, and pesticides. Workers in shipping, automobile repair, shoe manufacture, and refining/transportation of oil and gasoline are routinely exposed to benzene fumes. U.S. occupational guidelines limit benzene exposure to one part per million (ppm), but many workers in developing countries are thought to be exposed to much higher levels of benzene.

While it is well documented that long-term exposure to high levels of benzene reduces white blood cell counts and can cause leukemia in people, the impacts of exposure at levels below 1 ppm in the air are uncertain. Dr. Martyn Smith, Program Director of the University of California-Berkeley SBRP, and Dr. Stephen Rappaport, of the University of North Carolina-Chapel Hill SBRP, are collaborating with researchers from the National Cancer Institute and the Chinese Center for Disease Control to study the impacts of long-term exposure to low levels of benzene.

They conducted a cross-sectional study in a region near Tianjin, China including 250 shoe workers exposed to benzene-containing glues and 140 unexposed age- and sex-matched controls who worked in three clothes-manufacturing factories. They conducted extensive exposure assessments for 16 months, testing air samples in the factories as well as at each worker's home. Using blood and urine samples, the researchers linked individual air-monitoring data to end-points including white blood cell and platelet counts, lymphocyte subsets and progenitor cell colony formation.

As expected, workers exposed to benzene at levels of 1 ppm and higher had fewer total white blood cells, granulocytes, lymphocytes, B cells, and platelets than did unexposed workers. The researchers also found that compared to controls, *workers exposed to less than 1 ppm benzene had significantly decreased numbers of all types of white blood cells and platelets*. On average, these workers had 15% to 18% fewer granulocytes and B cells than unexposed workers, even after controlling for smoking and other potential confounding factors.

Because benzene affected nearly all blood cell types, the researchers suspected that benzene was toxic to progenitor cells – the unspecialized "parent" cells from which all other blood cells develop. They cultured samples from exposed workers and controls using colony-forming assays to measure the proliferative potential of progenitor cells. The scientists observed highly significant, *dose-dependent* decreases in colony formation of progenitor cells from exposed workers. Further, benzene caused a greater proportional decrease in colony formation than in levels of differentiated white blood cells and granulocytes, suggesting that *early progenitor cells are more sensitive than mature cells* to the toxic effects of benzene. This is the first study to find that benzene exposure affects the ability of progenitor cells to grow and multiply in humans.

The researchers then examined the influences of genetic variation in three enzymes responsible for activating and detoxifying benzene. They found that exposed subjects with variation in two enzymes (*MPO* and *NQO1*) were especially susceptible to benzene-induced lowering of white blood cell counts.

The results of this study highlight the importance of investigations into long-term health effects, including increased occurrence of blood diseases such as leukemia, in workers exposed to low levels of benzene. This study also shows the importance of careful documentation of exposure levels among all study

participants. By repeatedly measuring the personal exposures of the workers in this study, the researchers were able to minimize measurement errors that have obscured effects of low exposure to benzene in most previous investigations.

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To learn more about this research, please refer to:

Qing Lan, Luoping Zhang, Guilan Li, Roel Vermeulen, Rona S. Weinberg, Mustafa Dosemeci, Stephen M. Rappaport, Min Shen, Blanche P. Alter, Yongji Wu, William Kopp, Suramya Waidyanatha, Charles Rabkin, Weihong Guo, Stephen Chanock, Richard B. Hayes, Martha Linet, Sungkyoon Kim, Songnian Yin, Nathaniel Rothman, Martyn T. Smith. December 3, 2004. Hematotoxicity in Workers Exposed to Low Levels of Benzene. *Science* 306(5702): 1774-1776.