Environmental Health:

Implications of Benzene Exposure in China

by Sarah Yang

A new study of factory workers in China, led by researchers at the School of Public Health, the National Cancer Institute (NCI) and the Chinese Center for Disease Control and Prevention, has found that people exposed to low levels of the chemical benzene in the workplace had significantly lower blood cell counts compared to workers who were not exposed.

The researchers found that white blood cell and platelet counts were lower even with exposure levels below one part benzene per million parts air, or 1 ppm. They also found that benzene exposure significantly lowered the number of progenitor cells, which include stem cells, in the blood. These stem and progenitor cells are precursors to all blood cells.

"We need more studies to fully understand what these changes mean," says Martyn T. Smith, Ph.D., professor of toxicology and a senior author of the paper. "We need to look into what other kinds of biologic changes may be happening after benzene exposure in the bone marrow where blood cells are formed."

The study, published in the Dec. 3, 2005, issue of the journal *Science* and sponsored by the National Institutes of Health (NIH), was conducted in Tianjin, China, from 2000 to 2001. Researchers compared blood and urine samples from 250 people exposed to low levels of benzene in shoe manufacturing factories with a control group of 140 people working in clothing factories who were not exposed to benzene. They also monitored the levels of benzene in the air over the course of 12 to 16 months.

"Most of the prior studies focused on exposures to higher levels of benzene at work," says Luoping Zhang, Ph.D., a researcher at the School of Public Health and co-lead author of the study. "Our study found that benzene had an impact on blood cell counts at lower levels of exposure."

Zhang has been working with Smith on benzene-related studies in China since 1992. She adds that this study is the first to find that benzene exposure affected the ability of progenitor cells to grow and multiply in humans.

The findings on progenitor cells strengthens the link between benzene and leukemia, a cancer that begins with mutations in blood stem cells, according to the researchers.

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Benzene is a carcinogen regulated in the United States by the Environmental Protection Agency (EPA). It is a clear, colorless liquid that evaporates easily into the air, occurs naturally in crude oil and is present in refined gasoline. Benzene is also used as a solvent in paints, adhesives, and paint removers, but use of the chemical for those purposes has decreased in recent years in the United States. It is also found in tobacco smoke.

People can be exposed to benzene by smoking, breathing second-hand smoke, pumping gasoline, driving, and from air pollution. Elevated levels of benzene can occur in the air around gas stations, areas of high car traffic, and industrial plants that either produce or use it.

The EPA limits the use and release of benzene, and regulations set by the Occupational Safety & Health Administration limit workplace exposure to a maximum of 1 ppm averaged over an eight-hour workday.

In addition to measuring blood counts, the researchers examined inherited differences in genes that are involved in the metabolism of benzene in the body. They found that people with certain genetic traits were especially susceptible to the toxic effects of benzene on blood cells.

Specifically, benzene-exposed workers with a genetic variant in the myeloperoxidase (MPO) gene had significantly lower white blood cell counts than exposed workers without this variant.

It was Smith's first doctoral student at UC Berkeley, David Eastmond, Ph.D. '87, who discovered in 1986 that the enzyme MPO could metabolize benzene into toxic substances known as quinones. Eastmond is now a professor of toxicology at UC Riverside.

"MPO is critical because benzene itself is not the toxic agent in the body," says Smith. "It is when benzene is oxidized into toxic metabolites that it becomes harmful."

The study also included people with a variant in a gene called NQO1, which the Smith lab has studied for many years. NQO1 is considered protective against the damaging effects of benzene exposure because it detoxifies quinones and associated free radicals. However, for reasons that are not completely understood, people with a variant form of NQO1 were found to be more susceptible to benzene toxicity in this study.

"These results clearly support the need for more research on genetic susceptibility to benzene toxicity," says Smith.

The new findings build upon prior studies on benzene exposure in industrial workers in China. Those studies linked average benzene exposure levels of less than 10 ppm to risk of a range of blood-borne tumors and related disorders and to specific types of chromosome damage related to leukemia.

But the researchers point out that studies on the effects of low benzene exposure have been contradictory and that the results from this study must be independently confirmed. Nevertheless, they say it is important to examine long-term health effects, such as increased occurrence of serious diseases of the blood system, including leukemia, in workers exposed to low levels of benzene.

The research team also included investigators from the University of North Carolina at Chapel Hill and the New York Blood Center. Weihong Guo, M.S. '04, an assistant specialist in Smith's lab at the School of Public Health, also coauthored the study and helped collect the samples in China.