AMERICAN JOURNAL OF INDUSTRIAL MEDICINE 29:225-226 (1996)

EDITORIAL

Benzene and Blood: One Hundred Years of Evidence

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KEY WORDS: benzene, leukemia, lymphoma, aplastic anemia

In 1977 we shall mark the one-hundredth anniversary of the publication of the first case report describing hematologic toxicity in a worker exposed to benzene (LeNoir and Claude, 1897). In 1998, we shall observe the seventieth anniversary of the first report clearly associating benzene with leukemia (Delore and Borgomano, 1928).

In the century that has passed since the seminal observation that benzene is toxic to blood, a steadily accumulating body of data has shown to an ever-higher degree of certainty that benzene can cause a broad range of hematologic dysfunction, including all types of leukemia, lymphomas, myeloid metaplasia, and aplastic anemia (Young, 1989). These etiologic associations are substantiated by case reports, epidemiologic investigations, and laboratory studies. Benzene has been declared a proven human carcinogen by the International Agency for Research on Cancer, by the U.S. Environmental Protection Agency, by the United States Occupational Safety and Health Administration, by the National Institute for Occupational Safety and Health, and by occupational health and safety agencies around the world.

The three papers in this issue of the Journal reconfirm benzene's ability to cause a wide range of hematologic toxicity, including malignancy. They clearly show that benzene can cause dysfunction of synthesis in all blood-forming elements. The effect can occur quite early in cell development, in some instances at the stem cell level, and is seen even at very low levels of exposure. In the paper by Yin et al., (1996), a statistically significant excess of deaths was noted for leukemia, malignant lymphoma, and non-neoplastic diseases of the blood. Risk was elevated for all lymphohematopoietic malignancies, malignant lymphoma, and leukemia. Among the leukemia subtypes, only in the case of acute myelogenous leukemia did the excess achieve statistical significance at the 5% level, but nonsignificant excesses were noted for chronic myelogenous leukemia and for lymphocytic leukemia. Significant excesses were noted also for aplastic anemia and for myeloid metaplasia.

The Rothman et al (1996) paper provides strong evidence for a dose-response relationship between benzene exposure and hematotoxicity, and identifies decline in the absolute lymphocyte count as particularly sensitive to benzene exposure, thus confirming an important finding by Goldwater in 1941. In spite of industry's frequent claim that only acute myelogenous leukemia should be considered caused by benzene exposure, this effect on lymphocytes at low levels of exposure establishes further biologic plausibility for the observed etiologic association between benzene and lymphocyte-derived tumors.

The Rothman et al., results are corroborated by the positive findings of Ward et al., (1996). Ward and colleagues examined the effect of benzene on blood counts, but had data available on only total white and total red blood cell counts for the U.S. rubber worker's cohort. The strong negative dose-response relationships that are reported in this group between benzene and all white cells may actually underestimate the association between benzene exposure and depressed lymphocyte counts.

The tragedy of benzene is that it has taken so long for science to be translated into protective action. Many thousands of workers and other persons in nations around the world have suffered unnecessarily and died prematurely

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Accepted for publication November 20, 1995.

while regulatory agencies, industry, and the courts debated the carcinogenicity of benzene and argued about the need for protective regulation (Nicholson and Landrigan, 1989). In the current era of global proliferation of toxic chemical and hazardous technologies, all who are involved in the production and use of benzene have a heavy responsibility and a duty to protect their workers and the general public against this highly toxic and carcinogenic compound. The debate over whether benzene is carcinogenic has long since ended, and controversy about the need to protect humans against benzene must not continue.

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