Angiosarcoma of the Liver Among Polyvinyl Chloride Workers — Kentucky

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Between September 1967 and December 1973, 4 cases of angiosarcoma of the liver were diagnosed among men employed in the polyvinyl chloride polymerization section of a B.F. Goodrich plant near Louisville, Kentucky. This section of the plant began operations in 1938. It employs about 270 persons and produces polyvinyl chloride as well as a variety of copolymers by polymerization of vinyl chloride monomer. All 4 men had worked continuously in the section for at least 14 years prior to onset of illness (Table 1); all 4 had worked directly in various phases of the polymerization process.

Case 1 presented in August 1967 with an epigastric mass and thrombocytopenia. An exploratory laparotomy was performed in September 1967; liver biopsy revealed angiosarcoma. Case 2 presented in January 1970 with gastrointestinal (GI) bleeding. Recurrent bleeding in May 1970 led to an exploratory laparotomy at which time a diagnosis of angiosarcoma was made on liver biopsy. Case 3 presented in January 1964 with GI bleeding which recurred in May 1965 with signs of portal hypertension. A portacaval shunt was performed, and liver biopsy yielded a diagnosis of cirrhosis. Repeat biopsies in October 1970 and September 1972 confirmed this diagnosis. Autopsy in March 1973 revealed angiosarcoma. Case 4 presented in July 1973 with hepatosplenomegaly, weight loss, and jaundice. Two liver biopsies were interpreted as showing severe cirrhosis. Autopsy in December 1973 revealed angiosarcoma.

In each case, pathologic material revealed the presence of extensive cirrhosis of a non-alcoholic type in addition to angiosarcoma. In 2 cases, the diagnosis of angiosarcoma was made only at autopsy, cirrhosis having been diagnosed 7 years before in Case 3 and 5 months before in Case 4. None of the patients gave histories of prolonged alcohol use or exposure to hepatotoxin outside their work place. In particular, none had ever had exposure to thorium dioxide or to arsenic, two materials known specifically to induce hepatic angiosarcoma in man (*1,2*).

Table 1
Cases of Angiosarcoma of the Liver among Polyvinyl Chloride Workers
B.F. Goodrich Plant
Louisville, Kentucky

Case	Age at illness onset	Date of			Years worked with PVC before illness
		Illness onset	Diagnosis	Death	
1	43	Aug. 1967	Sept. 1967	Jan. 7, 1968	17
2	36	Jan. 1970	May 1970	Sept. 27, 1971	14
3	41	Jan. 1964	Mar. 1973	Mar. 3, 1973	14
4	58	July 1973	Dec. 1973	Dec. 19, 1973	27

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Editorial Note: Angiosarcoma of the liver is an exceedingly rare tumor. It is estimated that only about 25 such cases occur each year in the United States. Four cases, therefore, among a small number of workers at a single plant is a most unusual event, and one which raises the possibility of some work-related carcinogen, conceivably vinyl chloride itself. Although no data are yet available concerning the occurrence of angiosarcoma among workers at other vinyl chloride plants in the United States, it seems distinctly possible that the problem may be industry-wide. Epidemiologic studies have started to determine the extent of the problem in the United States, with respect both to angiosarcoma of the liver and to its possible relationship to post-toxic cirrhosis.

Published data concerning the potential hepato-toxicity and oncogenicity of vinyl chloride are limited. Studies in Germany have suggested a link between hepatic damage and occupational exposure to vinyl chloride (*3*), while Italian workers have suggested that vinyl chloride may cause a wide variety of tumors in animals (*4*). The chemical concentrations used in these latter experiments, however, far exceed levels likely to be encountered in industrial environments. Efforts to confirm such observations and to measure effects at lower dose levels are now in progress.

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Editorial Note—1997

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Workers constitute the segment of the U.S. population most heavily exposed to chemical toxins and physical agents. Because of their intense and prolonged exposures compared with the general public's, workers generally develop illnesses of toxic etiology more frequently, more quickly after the introduction of new chemical compounds, and in more severe forms.

Work-related diseases encompass a broad range of human illness (*1*). For example, chronic bronchitis frequently occurs in coal miners; skin cancer in farmers; bladder cancer in dye workers exposed to aniline compounds; leukemia and lymphoma in chemical workers exposed to benzene; kidney failure in lead workers; impaired reproductive function in workers exposed to lead and certain pesticides; and chronic disorders of the musculoskeletal system in workers who sustain repetitive trauma.

The diagnosis of occupationally associated disease often is difficult (*2*). For most diseases, a case of occupational origin is not clinically distinguishable from illness resulting from other etiologies. Informed suspicion is therefore essential to recognize occupational disease, and a careful history of occupational exposure is the critical diagnostic instrument. In the initial diagnostic interview of each new patient, the physician must obtain at least a brief history of occupational exposures. Modification of the concept of the sentinel health event (SHE) (*3*) has further assisted physicians in establishing linkages between occupational exposures and disease (*4*).

A SHE has been defined as "an unnecessary disease, disability, or untimely death whose occurrence signals a failure of prevention" (*3*). Examples in general medicine include maternal deaths during childbirth, outbreaks of cholera, or a single case of poliomyelitis. To extend the concept of the SHE to the workplace, a "sentinel health event (occupational)" (SHE[O]) is analogously defined (*4*) as "an unnecessary disease, disability or untimely death which is occupationally related." Recognition of a SHE(O) requires clinical astuteness and attention to the exposure history. Typically, the occurrence of a SHE(O) stimulates further investigation or research and may trigger regulatory or other targeted preventive action.

This *MMWR* report on angiosarcoma of the liver in vinyl chloride polymerization workers represents a splendid description of a SHE(O). This report marked the first recognition of the carcinogenicity to humans of vinyl chloride monomer (VCM), the highly reactive gas to which workers were exposed in the B.F. Goodrich plant near Louisville, Kentucky. The initial observation was made by John Creech, M.D., the plant physician, and Maurice Johnson, M.D., the corporate medical director. These physicians had evaluated three men with angiosarcoma of the liver during a 2-year period (*5*). They realized, through careful history-taking, that all of the men with this rare malignancy were employed in the same department of the plant.

Publication of this report and a related journal article (*5*) stimulated a series of clinical investigations, epidemiologic studies, and toxicologic analyses. Henry Falk, M.D., an Epidemic Intelligence Service (EIS) officer in the Cancer and Birth Defects Division in CDC's Bureau of Epidemiology, was assigned by his Division Director, Clark W. Heath, Jr., M.D., to investigate this outbreak. Working with Richard Waxweiler, Ph.D., of the National Institute for Occupational Safety and Health, Hans Popper, M.D., of the Mount Sinai School of Medicine, and Louis Thomas, M.D., of the National Cancer Institute, Dr. Falk confirmed the existence of the outbreak and also discovered a premalignant lesion—idiopathic hepatic fibrosis—in additional members of the population heavily exposed to vinyl chloride monomer (VCM) (*6*). This work stimulated a major international conference that was convened at the New York Academy of Sciences by Irving Selikoff, M.D. (*7*), at which the carcinogenicity of VCM was confirmed. VCM is now universally considered to be a highly potent chemical carcinogen (*7*).

This recognition of the carcinogenicity of VCM also stimulated intense regulatory activity (*8*). To prevent future cases of VCM-associated angiosarcoma, the Occupational Safety and Health Administration in 1974 proposed a 500-fold reduction in the occupational exposure standard for VCM gas—from 500 parts per million (ppm) in air to 1 ppm. The plastics-manufacturing industry immediately objected that such reduction was not possible and would drive the vinyl chloride polymerization industry overseas. An industry-sponsored study estimated that the costs to comply with the proposed new standard would exceed $25 billion (*8*). Within the year, however, a ma-

jor plastics manufacturer announced development of a novel closed-loop polymerization process that greatly reduced atmospheric releases of VCM and almost completely eliminated worker exposures. The manufacturer patented this system and subsequently licensed it to other manufacturers at substantial profit. The VCM standard of 1 ppm remains in force today (*9*) and is readily achieved in the workplace. New cases of hepatic angiosarcoma in vinyl chloride polymerization workers have been virtually eliminated (*10*).

This episode, one of the earliest reports of an occupational disease outbreak published in the *MMWR*, underscores the importance of informed clinical observation in the recognition of work-related illness. Furthermore, the regulatory actions precipitated by this report and the ensuing investigation of this episode illustrate that a safe working environment and economic progress are not mutually exclusive. When well-conceived protective standards are accepted with good will and ingenuity is used to encourage compliance with those standards, then job safety, economic advances, and a healthy environment can comfortably co-exist.

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