

ELAINE B. PANITZ M. D.
OCCUPATIONAL AND ENVIRONMENTAL MEDICINE

TELEPHONE
(609) 448-3737

EAST WINDSOR PROFESSIONAL PARK
ONE MILE ROAD EXTENSION
HIGHTSTOWN, NEW JERSEY 08520

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Ronald E. Grayzel, Esquire
96 James Street
Edison, NJ 08820

Re: John Byoris

Dear Mr. Grayzel:

At your request, I have reviewed the medical records and occupational history, supplied by your office, regarding John Byoris, deceased since 9/4/82.

History of Final Illness

Mr. Byoris was a 59-year-old white hypertensive male laborer, working for Witco Chemical Company, when he became ill in April 1982. Initial evaluations revealed fever of unknown origin, anemia, a 40 pound weight loss, and an elevated LDH blood level.

Admission to Perth Amboy General Hospital in June 1982 revealed extensive enlargement of lymph nodes in the abdomen. Attempts to obtain tissue for diagnosis were initially unsuccessful. After 4 weeks of steroid therapy, a laparotomy produced tissue that was diagnosed as a malignant lymphoma ("histiocytic" type, now referred to as "diffuse large cell" type).

Mr. Byoris was treated with chemotherapy but died on 9/4/82 after progressive bone marrow and renal failure. Gross findings at autopsy included: an enlarged heart with slightly enlarged chambers but normal wall thickness, moderate atherosclerotic change in the coronary arteries, a mottled pleural surface with a moderate amount of anthracotic pigment, multiple matted anthracotic lymph nodes around the trachea, retroperitoneal hemorrhagic tissues, and superficial ulcers of the stomach lining.

Microscopic autopsy findings included moderate to severe atherosclerosis of the coronary arteries, mild anthracosis in the lung parenchyma, and deteriorated, scarred tissues in the bone marrow and supporting tissues about the intestines and pancreas. These damaged tissues no doubt represented the lymphoma tissue after treatment with chemotherapy.

Occupational History

According to information provided by your office, Mr. Byoris was employed at Witco Chemical, Perth Amboy, NJ, from 1962 to 1982. During his years at the plant, Mr. Byoris worked as a laborer in the Pioneer Division's asphalt production area. He spent approximately 2 days each week as a mechanic's helper, cleaning out tanks used to store flux oil (the petroleum residuum that is converted to asphalt by an air-blowing process). It was his job to climb inside the unventilated tanks, without respiratory protection, and scrape out accumulated "coke" on the tank surfaces. He performed this operation by hand, using scrapers. Such cleaning operations took anywhere from 1 to 7 days to complete, and reportedly involved exposure to "large amounts of dust and fumes" within the tanks.

In 1976 the asphalt plant was closed and Mr. Byoris became a forklift operator. He apparently operated his forklift in areas of the plant which have subsequently been found to be highly contaminated with polychlorinated biphenyls (PCBs), by the New Jersey Department of Environmental Protection. DEP claims that soil borings from parts of the Witco property showed levels in the thousands of parts per million, or up to 3.5% of the soil.

DISCUSSION

Malignant Lymphomas

The lymphomas are a group of malignant diseases affecting the lymphoreticular system, usually arising in the lymph nodes. The lymphomas are usually classified as either Hodgkin or non-Hodgkin lymphoma, depending on histologic appearance. There are currently some 12 different varieties of nonHodgkin lymphoma, of which Mr. Byoris' tumor ("histiocytic" or large cell) is one.

For a number of years, investigators have suspected that some malignant lymphomas have an environmental etiology. This suspicion has stemmed from the "clustering" of lymphoma cases among people who live together, whether genetically related or not, and among people in the same geographical location. The incidence of malignant lymphomas has also been noted to be increasing around the world since 1975.

Independent researchers in the cancer field believe that some lymphomas are associated with chemicals in the workplace. This belief has grown steadily since the 1960's, from epidemiologic observations around the world, and in a variety of occupational settings.

A significant increase in the number of malignant lymphomas has been reported a) in the petrochemical and rubber industries [Thomas 1982 JOM 24:135, MonMichael 1975 JOM 17:234, Monson 1978 JNCI 61:1047], b) among chemists and those who work with organic solvents [Li 1969 JNCI 43:1159, Clin 1973 Lancet 2:916, Clin 1980

Env.Res.22:154], c) among woodworkers and those using wood preservatives such as pentachlorophenol [Erikson 1981 BJIM 38:27], d) in workers exposed to phenoxy acid herbicides such as 2,4,5-T [Hardell 1981 BJC 43:169], e) in plumbers and pipefitters fabricating plastic pipe and using solvents [Dolan 1983 JCM 25:613], and f) in anesthesiologists using multiple chemical agents [Vessey 1978 Anaes. 33:438].

Although an increase in lymphomas is noted to occur in these occupational groups with multiple chemical exposures, no single agent has been proven conclusively to be causative in such groups. Benzene has long been shown to cause hematologic disorders in various worker groups. Interestingly, there have also been case reports suggesting that benzene affects the lymphoreticular system (as well as the hematopoietic system) leading to lymphomas and related disorders (see below). Several studies have suggested an association between malignant lymphoma and occupational exposure to asbestos [Gerber 1978 Am.J.Clin.Path. 53:204, Kagan 1979 Am.J.Med. 67:325, Ross 1982 Lancet 2:1118], and asbestos is known to affect the immune system in man.

Predilection for lymphomas in man appears to be associated with abnormalities of the immune system, whether genetically or environmentally acquired. It is speculated that lymphomas arise through chemical alteration of the immune system.

For example, the therapeutic use of immunosuppressive chemicals in man (in transplantation, autoimmune disorders, cancer) markedly increases the risk of malignant lymphoma. The risk of developing non-Hodgkin lymphoma is multiplied some 60 times in transplant patients receiving immunosuppressive drugs. Embryologically-related tumors, known as soft tissue sarcomas, are also increased in such a setting. Remarkably, the induction (or latency) period required to increase the lymphoma risk has been demonstrated to be as little as one month. This short latency period stands in contrast to the long latencies associated with other carcinogens in man.

Petroleum Residuum

Petroleum residuum ("flux oil") is the material remaining after treatment of crude petroleum in an oil refinery. It is a mixture of materials of poorly defined and indefinite hydrocarbon composition. Its cousins include such complex mixtures as soots, pitch, coal tar and products, creosote, shales, mineral oils, and cutting oils.

Depending on the boiling point reached during distillation, petroleum residuum may contain up to 50% aromatic hydrocarbons, widely held to be carcinogenic in both animals and man. Aromatic hydrocarbons are characterized by the presence of one or more benzene rings. They are classified into three main groups, depending on number of benzene rings and binding:

a) benzene and its derivatives, b) polyphenyls (including polychlorinated biphenyls or PCBs), and c) polynuclear aromatic hydrocarbons (or PAH). Although distillation of coal in the coking process was the original source for aromatic hydrocarbons, at the present time the petrochemical industry is the major source of such aromatic compounds.

Benzene

Although most benzene is driven off from crude petroleum in the oil refinery, petroleum residuum may continue to evolve small amounts of benzene and other volatiles, which can accumulate inside unventilated tanks such as those cleaned by Mr. Byoris. While most petrochemical workers today avoid significant benzene exposures because of largely outdoor work settings, those who work indoors or in unventilated situations (shoemaking, rubber manufacture) have continued to demonstrate benzene-related health effects, including increased lymphomas [Delzell 1981 JOM 23:677]. It is because of the possible accumulation of aromatic volatiles such as benzene that management is constrained to "sniff test" such tanks before the entry of workers. The major routes of exposure is through inhalation and skin absorption.

Benzene is well-known for its effects on the bone marrow in workers chronically exposed: aplastic anemia and various forms of leukemia. Animal studies have demonstrated that benzene also causes changes in the lymph nodes of rats (Wirtschafter, Z.T., et.al. Arch. Path. 67:146, 1960). A relationship to lymphoma in man was first suggested by Bousser in 1947, who reported a case of diffuse histiocytic lymphoma in a worker after 3.5 years of chronic benzene exposure. In 1980, Aksoy (Haematologica 65:378) reported 4 cases of malignant lymphoma in chronically exposed (10-17 years) shoe-workers, one of which was a diffuse histiocytic lymphoma in a worker 42 years old.

Certain other occupational groups, such as chemists, with presumed chronic exposure to benzene, have demonstrated increased occurrence of lymphoma (Olin 1980 Env. Res. 22:154, Olin 1976 Lancet 2:916, Li 1969 JNCI 43:1159, Viglianni 1976 Env. Res. 11:122, Infante 1977 Lancet 2:76, Vianna 1979 Lancet 1:1394).

Polychlorinated Biphenyls and Dioxins

Polychlorinated biphenyls (PCBs) were found in high concentrations on the Witco property. PCBs are generally considered to be contaminated with polychlorinated dibenzodioxins, the most toxic of which is tetrachlorodibenzodioxin, or TCDD, referred to often as "dioxin". I do not know of TCDD levels measured on Witco property, but other areas around the USA with heavy PCB contamination have demonstrated TCDD levels from 1 to 1000 parts per billion. TCDD is a potent animal carcinogen, and recent government publications have indicated that "soil levels greater than 1 part per billion pose a level of concern" to human beings.

TCDD is considered to be the most toxic synthetic compound known, and it is highly persistent in the environment. In animals and people it concentrates mainly in the liver, fat, thymus, and spleen. Animal studies have demonstrated that immunotoxicity is a serious health effect at low doses of TCDD: atrophy of lymphoid tissues and suppression of humoral immune function, with decreased resistance to infection (Dean 1966 J. Reticuloendothel. Soc. 28:571, Vos 1981 Tox.App.Pharm. 61:18, Koller 1973 Am.J.Vet.Res. 34:1605, Thomas 1978 Tox.App.Pharm. 44:41, Loose 1981 Env.Health Persp. 39:79).

It is noteworthy that workers exposed to PCBs (and presumably TCDD), both in Sweden and in the USA, have demonstrated an increase in lymphomas and/or soft tissue sarcomas, tumors that are known to occur in other immunocompromised patients (see above, Malignant Lymphomas).

Exposure to TCDD occurs through three routes: dermal absorption through direct contact with the soil, ingestion of soil, and the inhalation of dust to which TCDD is attached. Anywhere from 1 to 10% of TCDD in the soil may be absorbed through the skin, and may increase with higher soil concentrations. Some 30% of ingested TCDD is absorbed into the body. Inhaled TCDD is deposited in the respiratory tract or ingested after being brought up from the respiratory tract. As a forklift driver moving about the Witco property, it is probable that Mr. Byoris had significant inhalation and ingestion of airborne TCDD-laden dust. There may also have been some dermal absorption.

Polynuclear Aromatic Hydrocarbons

Hydrocarbon mixtures, such as petroleum residuum, are widely considered to contain substances that are thought or known to be carcinogenic in animals and in man. They are known to contain polynuclear aromatic hydrocarbons, or PAH, a group of chemicals that have been linked to human lung cancer. Certain members of the PAH family, notably benzo(a)pyrene, 3-methylcholanthrene, and dibenzanthracene, have exhibited marked carcinogenic activity in animals. Tumors have developed in rodents within weeks or months after minute exposure to these compounds. In fact, members of the PAH family were among the first pure chemicals used for cancer induction in animals.

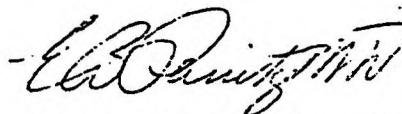
A recent study has demonstrated that mice pretreated with 3-methylcholanthrene (member of PAH family) exhibit much greater bone marrow chromosomal damage when subsequently exposed to benzene (Cad-el-Karim 1984 Mut. Res. 135:225). Such synergism is likely to exist among numerous carcinogens, greatly enhancing the toxicity of exposures (such as Mr. Byoris') to a mixture of chemicals.

SUMMARY

Mr. Byoris was exposed to petroleum residuum and PCBs over a period of years while working for Witco Chemical from 1962 to 1982. During 1982 he developed a malignant lymphoma at age 59. The tumor apparently had its origins in retroperitoneal lymphatic tissues. Mr. Byoris received chemotherapy but developed progressive bone marrow suppression and renal failure. He died less than 5 months after the onset of symptoms.

Mr. Byoris spent a number of years cleaning out unventilated tanks that contained petroleum residuum and accumulated "coke". He worked many hours inside these tanks with no respiratory protection. It is my feeling that his exposure to aromatic hydrocarbons in this setting was likely to have been heavy, and that he also had heavy exposure to PCB-laden soil over a period of years. In my opinion, based on reasonable medical probability, the exposures to aromatic hydrocarbons and PCBs (TCDD) were substantial contributing factors to development of malignant lymphoma in Mr. Byoris.

Yours truly,



Elaine B. Panitz, MD

EBP/jp
Enclosure