SENTINEL DISEASES

PLAINTIFF'S EXHIBIT

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Letters to the Editor

Identification of Occupational Settings With Very High Risks of Lung Cancer

Sir: We would like to comment on your editorial in the April 1979 issue of *JNCI* entitled, "The Case for Cancer Prevention," in which you state: "There seem to be no immediate opportunities for large-scale cancer prevention strategies that are not already well known. . . ." We suggest that probably some worthwhile ideas for strategies have been thought of by people who would be happy to air them if a suitable place to do so were available.

For example, at this institute we have been interested in the temporal aspects of tumor induction by carcinogens for many years.[1] In the course of an epidemiologic study on lung cancer in workers exposed to the very potent carcinogen bis(chloromethyl) ether (BCME), we were struck by the youth of some of the workers with lung cancer at one plant where 4 of the 23 patients were less than 40 years of age.[2] The chance of finding lung cancer in such young men is very low; e.g., in New York State only 0.6% of lung cancers occur in men between the ages of 35 and 40 years.[3] The induction of lung cancer at an early age is consistent with considerable evidence in humans and other animals that the higher the level of exposure to a carcinogen, the sooner the cancer cases are observed to appear.[1] The type of cancers that these workers exposed to BCME developed was also striking. All of the patients, including those under 40 years of age, developed either squamous carcinoma of the bronchus or small-cell undifferentiated carcinoma of the bronchus.[4] According to Kreyberg,[5] only a minority (≈20%) of lung cancers that occur in persons under 40 years of age are of the aforementioned types. Chemical and physical agents that cause lung cancer in humans, e.g., cigarette smoke,[7] radon daughters in uranium mines,[6] and BCME,[4] commonly produce squamous or small-cell undifferentiated carcinoma. Hence the occurrence of squamous carcinoma or small-cell undifferentiated bronchial carcinoma in persons under 40 years of age strongly suggests that they had intense exposure to a powerful carcinogen. Even with cigarette smoking, the occurrence of lung cancer in young people is not common. In British physicians taken as a group, who probably did not have high-level exposure to carcinogenic inhalants other than cigarette smoke, no patients under the age of 40 were found in a total of 201 lung cancer cases.[7] We recently learned of a second example of lung cancers in young chemical workers in a German plant where intense inhalation exposure to the carcinogen vinylidene chloride was associated with 5 lung cancer cases, 2 of which occurred in workers under 40 years of age (Frentzel-Beyme R: Personal communication). The only situation in which sustained high-level inhalation exposure to respiratory carcinogens other than cigarette smoke is likely to occur is in occupational environments that are poorly controlled from the standpoint of industrial hygiene.

All of the previously mentioned instances suggest that we may have the ingredients for an efficient "alert" system for identification of situations with high-level carcinogen exposure to men (because of the relevance to the chemical industry) who are under 40 years old and who develop squamous or small-cell undifferentiated lung cancer. This alert system would be particularly effective if it focused primarily, but not exclusively, on cases that occur in nonsmokers; of the 4 lung cancer cases in young workers exposed to BCME, 2 involved nonsmokers.[4]

Such an alert system for the detection of high-level occupational respiratory carcinogen exposures would require a method for screening of very large populations because of the rarity of the cases of interest. This screening could be done through the use of cancer registries. For example, the New York, New Jersey, and Connecticut cancer registries contain about 10,000 cases of lung cancer in men each year. If we assume that 0.6% are under 40 years of age, this percentage would amount to 60 cases. This is a small number, but the small number would be an advantage because relatively little effort would be required to investigate them, and most likely the detection of occupational settings with exceedingly dangerous levels of carcinogen exposure could be accomplished. If only a few of these settings could be identified each year, the return in public health benefits would be great for a modest amount of effort.

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[1] ALBERT RE, ALTSHULER B: Considerations relating to the formulation of limits for unavoidable population exposures to environmental carcinogens. *In* Radionuclide Carcinogenesis (Sanders CL, Suscb RH, Ballou JE, et al, eds). AEC Symposium Series, CONF-720505. Springfield, Va.: Natl Tech Information Serv, 1973, pp 233-253

[2] PASTERNACK BS, SHORE RE, ALBERT RE: Occupational exposure to chloromethyl ethers: A retrospective cohort mortality study (1948-1972). J Occup Med 19:741-746, 1977

[3] Bureau of Cancer Control: Cancer incidence and mortality in New York State (exclusive of New York City). Albany, N.Y.: New York State Dept Health, 1976

[4] FIGUEROA WG, RASZKOWSKI R, WEISS W: Lung cancer in chloromethyl methyl ether workers. N Engl J Med 288:1096-1097, 1973

[5] KREYBERG L: Histological lung cancer types. A morphological and biological correlation. Acta Pathol Microbiol Scand [suppl] 137:1-92, 1962

[6] SACCOMANNO G, ARCHER VE, AUERBACH O, et al: Histologic types of lung cancer among uranium miners. Cancer 27:515-523, 1971

[7] DOLL R, PETO R: Cigarette smoking and bronchial carcinoma: Dose and time relationships among regular smokers and lifelong non-smokers. J Epidemiol Community Health 32:303-313, 1978

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By this example, we suggest that people might devise all sorts of cancer prevention strategies if they were encouraged to think about cancer prevention and if a suitable publication were available for discussion of prevention strategies.

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SIR: *In just a few paragraphs, Albert et al. raise four important issues. First, and most limited, is the significance of the specific example they cite. Their evidence is striking and should lead promptly to further study and, one may presume, to control of another occupation-related risk. Second, they express the need for an "alert" system for detection of large proportionate increases in rare tumors. One can only agree, though problems would be formidable. Such mechanisms have been discussed for several decades at least, without the development of a comprehensive workable system.*

The third issue may be the interpretation of my statement about "large-scale cancer prevention strategies." That statement still seems accurate, although I did not mean to imply that we should ignore numerically limited risks. Every carcinogenic hazard should be fully investigated and attacked, regardless of how few persons may be exposed. However, we must not let such work distract us from the greater problems that may cause far more illness and mortality.

Last is the question of publication of worthwhile ideas on strategies for the prevention of cancer. Outlets do exist. The Journal of the National Cancer Institute *is one of them, and we encourage the submission of soundly based, carefully reasoned, adequately documented discussions on all aspects of the control of cancer.*

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