Relationship of Industrial Carcinogens to Cancer in the General Population

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AWARENESS of environmental cancer and recognition and acceptance of the extent of this problem are increasing in the United States.

A rapidly growing accumulation of evidence suggests that industry-related or occupational cancer hazards carry as a corollary a similar, though diluted or attenuated, hazard for the general population. The industrialization of society during the past half century has resulted in certain new socioeconomic phenomena, one of which has been the concentration of population in close proximity to industrial sources of environmental pollution. This concentration of population and the recent advent of the atomic age, the era of synthetics, and the petroleum economy, when combined with epidemiological observations, indicate that a general population hazard is of more than theoretical significance.

This hazard may be evaluated by two complementary methods of study. The first is an epidemiological-statistical analysis of both occupationally and environmentally exposed persons, using morbidity and mortality data; the second is the experimental assessment of the carcinogenicity and carcinogenic potency of known and suspected materials in the environment. The summation of both approaches often permits of conclusions impossible with either approach alone. Questions as to the value of experimental studies may be disposed of on the basis of the knowledge that confirmed or highly suspect environmental carcinogens have been proved to be carcinogenic for appropriate animal species. For those substances in which carcinogenicity is still lacking suggestive confirmation, experimental studies have been essentially unsuccessful in terms of tumor production.

In those other instances in which proved experimental carcinogens have thus far failed to demonstrate an analogous human tumorigenic response, it must be remembered that latency or the initiation-promotion-tumor development sequence in human beings is a long one and substances such as plastics (*1*), selenium (*2*),

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and beryllium (*3*), which have been used to produce experimental cancers, are relative newcomers in quantity to the human environment.

Industry-related carcinogens may enter the general environment through the atmosphere, water supply, soil, foodstuffs, medicaments, cosmetics, and products of industrial manufacture.

Numerous hydrocarbon compounds, of both the aliphatic and aromatic type, are released into the atmosphere secondary to the combustion of solid or liquid fuels in both industrial installations and through the exhausts of gasoline and diesel engines. Arsenicals may reach the atmosphere secondary to the manufacture and use of arsenical pesticides and the smelting of arsenic-containing ores. Radioactive substances may pollute the atmosphere subsequent to nuclear explosions, radioactive ore mining and smelting, and radioactive product manufacture.

Water and soil pollution frequently occur secondary to petroleum and other hydrocarbon source manufacture and subsequent to the disposition of radioactive wastes.

A potential hazard occurring in foodstuffs exists in the as yet incompletely studied role of pyrolized fats in carcinogenesis and the presence of synthetic food dyes, which may possess certain carcinogenic properties.

Products of industrial manufacture for general population use continue to increase in the direction of the utilization of petroleum derivatives as the sources of numerous household substances and of macromolecular compounds in the form of synthetics and plastics.

In addition to the sources and their environmental sites, carcinogens may be classified on the basis of their chemical and physical state and of the target tissue. Chemically, they may not only be present as highly complex molecular organic structures but also as inorganic substances, such as chromium, nickel, and arsenic. Physically, they may be in the form of ionizing radiation. Of additional physical significance is the dynamic nature of chemical compounds. Any biological activity, proved or postulated, may be critically related to the physical nature of any suspected chemical, including, for example, such factors as state of adsorption, elutability, and particle size.

Target tissues for carcinogenic substances include the skin, bones, lungs, upper respiratory tract, liver, bladder, and hemopoietic tissue. The activity of these substances within specific organ sites may be on the basis of initial contact, such as soot on the skin; site of metabolism or detoxification, such as azo dyes in the liver; or site of concentration and elimination, such as aromatic amines in the genitourinary tract.

Analyses of population groups have not only shown a demonstrable difference in liability to cancer on a geographic and demographic basis, but individual groups in specific geographic areas frequently show variations in cancer incidence. One of the bases for subgrouping has been the socioeconomic levels of population segments. One of the common denominators in socioeconomic levels is the environmental spectrum to which members are exposed.

Industry-Related Carcinogens

A brief discussion of several specific industry-related materials shown to be either experimentally or clinically carcinogenic may serve to indicate the need for and method of study of additional potentially hazardous materials.

Arsenic has been demonstrated to be a relatively common atmospheric and water contaminant secondary to mining and milling operations of arsenic-contaminated ores. Chronic arsenicosis in exposed population groups with an excessive incidence of skin cancer has been described by investigators. Arsenic has also been incriminated as a potential skin cancer hazard when used medicinally. However, its role in carcinogenesis is still being debated, especially in relation to the development of lung cancer; as a contaminant of tobacco and as the possible modus vivendi of the Schneeberg and Joachimsthal lung cancers.

Beryllium shares with arsenic an as yet ill-defined though highly suspicious place in the spectrum of potential carcinogens. The experimental production of cancers combined with the report of "neighborhood cases" of berylliosis adjacent to areas where beryllium is used in industry removes the problem from one of strictly "in-plant" industrial significance (*4*).

That radiation is a hazard to the general population is attested to by the reports of the ex-

aggerated prevalence of leukemia in exposed residents of Hiroshima and Nagasaki subsequent to the bombings.

Estrogenic substances, food dyes, tobacco, heavy and light metals, macromolecular compounds, and polymers are some of the additional compounds in need of elucidation in terms of their hazard to the general population.

Air Pollution and Lung Cancer

The role of atmospheric hydrocarbon substances must be mentioned as they relate to the reported increasing incidence of lung cancer. In a study of polluted atmosphere and sources of atmospheric pollution in a large urban American community, many previously reported findings were confirmed and certain additional initial observations were made, all quite possibly related to the pathogenesis of lung cancer in man (*5*):

1. Soot-containing carcinogenic hydrocarbons of the dibenzanthracene series have been recovered from the atmosphere and their presence has been quantitated.

2. Sources of the atmospheric hydrocarbons have been defined, with gasoline and diesel engine exhausts and industrial effluents being demonstrated as some of the sources.

3. Extracts of both atmospheric soots and pollutant source materials have been successfully used in skin painting experiments to produce skin cancers in C57 black mice, a strain which is normally resistant to spontaneous cancer.

In addition to this confirmatory work, analytical and biological studies have resulted in the following new observations. First, oxidation products of short chain aliphatic compounds have been demonstrated in the atmosphere, and these, too, have been successfully used to produce skin tumors in mice. Second, these experimentally carcinogenic substances, as present in the atmosphere in highly polar aerosol form, may serve as potential eluting agents for the soot adsorbed carcinogens so that action on the bronchial mucosa by these hydrocarbons becomes theoretically possible.

These observations parallel most dramatically the increasing incidence of lung cancer. The period since the initiation of large-scale introduction of industrial pollutants into the atmosphere is entirely compatible with the latent period now generally accepted for the development of lung cancer, which ranges from 10 to 40 years. Furthermore, they are congruous with the reported difference in frequency of urban and rural lung cancer. In rural areas, air pollutants are present in a diluted form, and the tumor-dose exposure of rural residents is on a lower level than that of urban residents, the latent period is prolonged, and the incidence is lower.

REFERENCES

(*1*) Oppenheimer, B. S., Oppenheimer, E. T., Stout, A. P., and Danishefsky, I.: Malignant tumors resulting from imbedding plastics in rodents. Science 118: 305–306, Sept. 11, 1953.

(*2*) Nelson, A. A., Fitzhugh, O. G., and Calvery, H. O.: Liver tumors following cirrhosis caused by selenium in rats. Cancer Research 3: 230–236, April 1943.

(*3*) Eisenbud, M., Wanta, R. C., Dustan, C., Steadman, L. T., Harris, W. B., and Wolf, B. S.: Non-occupational berylliosis. J. Indust. Hyg. & Toxicol. 31: 282–294, Sept. 1949.

(*4*) Hueper, W. C.: Occupational and environmental pulmonary cancer with special reference to pneumoconiosis. To be published in the Proceedings of the Seventh Saranac Symposium on Pneumoconioses.

(*5*) Kotin, P., Falk, H. L., Mader, P., and Thomas, M.: Aromatic hydrocarbons. I. Presence in the Los Angeles atmosphere and the carcinogenicity of atmospheric extracts. A. M. A. Arch. Indust. Hyg. 9: 153–163, Feb. 1954.

technical publications

The Social Worker's Role in Mental Health

Public Health Service Publication No. 351. 1954. 12 pages; illustrations. 10 cents.

This booklet develops the theme that mental health components are inherent in the practice of social work, regardless of specialization, and particularly in psychiatric social work. Consequently, the social worker is in an unique position to bring a mental health approach to his work with individuals and with families. It contains outlines of the various specialized fields of social work.

This booklet is the fourth in a series of five pamphlets which deal respectively with the role of the nurse, the policeman, the supervisor, the social worker, and the teacher in the mental health field.

Tuberculosis Beds in Hospitals and Sanatoria, April 1, 1954

Public Health Service Publication No. 412. 1954. 54 pages; tables. 40 cents.

The ninth edition of this index indicates that there are 1,124 institutions which provide care of some kind for tuberculous patients. Of these, 713 provide 115,157 beds for the care of tuberculous patients. The remaining 411 hospitals take patients for diagnosis, for surgery, or for emergency treatment pending transfer to other institutions but, in general, do not have a specific number of beds set aside for these purposes. Of the total number, 992 are non-Federal institutions (State, city, county, and district operated), and 132 are operated by the Federal Government.

In the continental United States alone there are 1,097 institutions with facilities for the care of tuberculous patients; 973 are non-Federal, of which 568 have 90,652 tuberculosis beds, and 124 are federally operated, 122 of which have 19,275 beds.

The index lists each institution and shows its rated capacity for tuberculous patients, and includes information about occupancy, type of hospital and ownership. A comparison is made with the occupancy information collected in April 1953 and new construction is discussed. Selected information is shown for each State.

The Teacher and Mental Health

Public Health Service Publication No. 385. 1954. 20 pages; illustrated. 15 cents.

The teacher's supportive role in helping the child meet his emotional needs is explained in this publication. It points out what some of the States and school systems are doing to provide teachers with a knowledge of the dynamics of mental health principles. Also, a list of books, pamphlets, reprints, and films on the subject of mental health is included.

This is the fifth and last pamphlet in a series of pamphlets which deals respectively with the role of the nurse, policeman, supervisor, social worker, and teacher in mental health.

State Heart Disease Control Programs as Planned for Fiscal Years 1954 and 1955

Public Health Service Publication No. 406. 1954. 33 pages; tables. 30 cents.

Presented in abstract form are the plans of the States, Territories, and the District of Columbia for their heart disease control programs covering, for the most part, the 2-year period beginning with the fiscal year 1954.

The abstracts are based on the State plans, required by the Federal Social Security Act of 1935, of all State agencies participating in grant programs administered by the Public Health Service. Program plans were submitted in either of two forms, the State making its choice: the old style annual combined report and plan; or the new narrative type plan—adopted in 1952—placing emphasis on planning on a program basis rather than on an organizational basis.

Because of differences in the States' presentations of detail and quantitative information, the abstracts in this publication are quite diverse, particularly with respect to specificity and elaboration of details. No attempt has been made to evaluate the program content in the abstracting. The proposed elements reported by the responsible State officials are presented concisely, giving the outline of each State health department's program for heart disease control.

The abstracts are arranged on a regional basis, conforming to the established regions of the Department of Health, Education, and Welfare, to relate the common problems existing among States located within specific regional areas. Selected administrative information, including placement of program responsibility and staff assignments, of each State's heart disease control program is shown in tabular form.

This section carries announcements of all new Public Health Service publications and of selected new publications on health topics prepared by other Federal Government agencies.

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The Public Health Service does not supply publications issued by other agencies.
