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March
Teratogens and Carcinogens

The relationship between congenital malformations and neoplastic diseases is discussed in a guest editorial by Miller (Clinical Epidemiology Branch, National Cancer Institute, Bethesda, Maryland). Children with ataxia-telangiectasia are predisposed to lymphoma while patients with xeroderma pigmentosum have a tendency to skin cancer. In both instances, the defect in DNA repair after damage by radiation is attributed to deficiency in endonuclease. The correlation between hereditary retinoblastoma and second primary tumors, especially osteosarcoma, is being assessed to determine whether a defect in DNA repair after radiotherapy accounts for greater susceptibility to second primaries. In addition, investigators have found that congenital cytogenetic abnormalities characterize persons at high risk for leukemia, congenital cell-mediated immunodeficiencies characterize persons at high risk for lymphoma, and urinary tract anomalies predispose to nephroblastoma.

From these cases, some generalizations about the origins of specific cancers can be made. Leukemia caused by environmental factors is associated with chromosome aberrations and, in the general population, is being linked with specific cytogenetic aberrations detected by new banding techniques.

Some teratogenic compounds have not been found to be carcinogenic in man. For example, polychlorinated biphenyls cross the placenta and concentrate in the fat of human milk, but no long-term effects in man have been demonstrated. Alternatively, some carcinogens are not known to be teratogenic in man; e.g., cigarette smoking by pregnant women has not been shown to produce congenital anomalies. Still other teratogens are carcinogenic. These include ionizing radiation, alcohol, hydantoin, androgens and diethylstilbestrol. Such studies of the relationship of germinal mutations on certain malformations and cancer have provided new insights into the process of carcinogenesis.

Gastric Cancer—An Assessment

The current treatment and prognosis of gastric cancer is reviewed by Carter (National Cancer Institute, Bethesda, Maryland) and Comis (Sidney Farber Cancer Center, Boston, Massachusetts). A decline in deaths from carcinoma of the stomach has been noted in the United States, Australia, Canada and England. In the Soviet Union, however, 30 percent of all cancers originate in the stomach, and the rate is even higher in Japan. The peak age for diagnosis of stomach
cancer is between 70 and 80 years, with 60 percent of all cases occurring in persons 60 to 70 years old. The chief hope for cure is surgical treatment, yet the five-year survival rate of approximately 13 percent has not improved in the past 20 years. The presence or absence of lymph node involvement is the greatest prognostic factor. Radiotherapy is seldom used except as a palliative measure for hemorrhage or pain; postoperative radiation has not been shown to increase survival rates.

The drugs most commonly used to treat gastric cancer are 5-fluorouracil and mitomycin C; 5-fluorouracil plus radiotherapy has been shown to enhance survival in patients with locally unresectable disease. A combination of 5-fluorouracil, mitomycin C and cytosine arabinoside has produced high response rates in Japan. This combination is used also at the Memorial Sloan-Kettering Cancer Center. The Mayo Clinic has reported a 41 percent response rate with 5-fluorouracil plus 1,3-bis(2-chloroethyl)-1-nitrosourea.

Although some good results have been reported, the use of chemotherapy as an adjuvant to surgery for gastric cancer requires further investigation. The lack of definitive conclusions regarding treatment, which may be due to faulty designs of clinical trials and inadequate chemotherapy, may permit insight into critical principles for the design of future combined modality therapies.

Effect of Intestinal Bacteria Antigens on Intestinal Epithelium

Van Bekkum and Knaan (Radiological Institute TNO, Rijswijk, The Netherlands) hypothesize that the presence of antigens on certain intestinal bacteria cross-react with antigens of the intestinal epithelium. They implanted fetal gut tissue of the parent strain or F₁ origin under the skin of (C57BL X CBA)F₁ mice. Thus intestinal tissue with and without microflora was present simultaneously in the same host. After palpable lumps developed, the hosts were subjected to lethal irradiation and given CBA bone marrow cells plus spleen cells intravenously. Acute graft-versus-host disease developed, as shown in histologic sections of the F₁ fetal gut implants and the host's own gut. Less damage occurred in the fetal CBA grafts.

Third National Cancer Survey

Data from the Third National Cancer Survey were discussed in two papers by Williams and associates (Biometry Branch, National Cancer Institute, Bethesda, Maryland). The first report describes the acquisition of epidemiologic information on 7,518 incident cases of cancer by interviews conducted during 1969-1971 and the analytic approaches used for interpretation of the data.

The second paper assesses the association of cancer sites with tobacco and alcohol consumption as well as the socioeconomic status of these patients. Age, race, sex, smoking and drinking habits, income, education, parity, foreign birth, marital status and geographic location were used as stratification variables to assess separate or combined effects and to examine results in different strata.

Cigarette smoking had a significant positive association with cancers of the lung, larynx, oral cavity, esophagus, stomach, pancreas, bladder, kidney and uterine cervix. Other forms of tobacco were associated with cancers of the oral cavity, larynx, lung and uterine cervix. Consumption of alcohol showed positive associations with cancers of the oral cavity, larynx, esophagus, colon, rectum, breast and thyroid gland. Both college education and high income had a high correlation with cancers of the breast, thyroid gland, uterine corpus and melanomas in males, but an inverse association with invasive tumors of the
uterine cervix, lung, lip-tongue and colon in females. College attendance had an inverse association with gastric cancer and a positive association with pancreatic cancer in males.

Carcinogenicity of Fibrous Glass
Stanton and co-workers (Laboratory of Pathology, National Cancer Institute, Bethesda, Maryland) believe that the carcinogenicity of asbestos and fibrous glass in man depends on its fine, long dimensions and durability rather than on its physicochemical properties. They implanted 17 fibrous glasses of different types or dimensions into the pleuras of female Osborne-Mendel rats and induced varying incidences of malignant mesenchymal neoplasms. The neoplastic response correlated well with the dimensions of the fibers; those 1.5 μ or less in diameter and more than eight μ long caused the largest number of pleural sarcomas.

It is reasonable to assume that dust containing fine, long, durable fibers is a potential hazard to man and should be regarded with caution. Tolerance levels for human exposure must take into account not only the variety of fiber but its dimensions as well. Future inhalation experiments should establish safety guidelines for areas where such fibers are used.

April
Cancer Incidence and Environment
In a guest editorial, Wynder (American Health Foundation, New York, New York) and Gori (National Cancer Institute, Bethesda, Maryland) submit data suggesting that most cancers today are induced by elements in man’s environment rather than by genetic or viral factors. Some of these environmental factors include: exposure to industrial materials such as polyvinyl chloride, asbestos and uranium dust; sunlight; smoking habits; dietary practices; alcohol intake; air and water pollution; and drugs such as the immunosuppressive types, estrogens and reserpine.

International comparisons of morbidity and mortality rates show that most cancers are related to man’s life-style; this life-style parallels the development of industrial societies. Wild animals and primitive societies, which may not be exposed to as many environmental carcinogens, have lower rates of certain types of cancer than do persons in highly industrialized countries.

Some individuals expose themselves to environmental carcinogens as a result of their choice of life-style. Thus they tend to ignore their own responsibilities and blame outside forces for harmful exposure. An individual can significantly limit his own risk by altering his life-style to give up habits that are detrimental to health. However, for the exposure to environmental carcinogens that cannot be controlled by the individual, public action is necessary and preventive measures should be introduced to protect society.

Cerebellar Gliomas in Children
A classification for cerebellar gliomas (excluding medulloblastomas) in children was derived by Winston and colleagues (The Children’s Hospital Medical Center, Boston, Massachusetts). Survival times and histologic features of this neoplasm in 132 children, whose initial operation for tumor was at the Children’s Hospital Medical Center between 1927 and 1968, were the basis of their division of this tumor into two major subgroups, gliomas A and B. Each had differentially distributed symptoms and clinical characteristics and differences in resectability. Glioma A contains any of these four histologic features: microcyst, leptomeningeal deposit, Rosenthal fiber or focus of oligodendroglia. Glioma B, clearly defined but histologically less uniform, encompasses features of perivascular pseudorosette, high cell density, ne-
crosis, mitosis and calcification. These two types account for 90 percent of the cerebellar gliomas in childhood. The 10-year survival of group A is 94 percent, whereas that of group B is 29 percent.

Possibly, individual or groups of histologic features will be used to improve prognostic accuracy for patients with cerebellar gliomas in the future.

Immunochemotherapy of Malignant Melanoma

Ghose and co-workers (Dalhousie University and Victoria General and Camp Hill Hospitals, Halifax, Nova Scotia) present results of treatment of 24 patients with clinically progressive non-ocular metastatic malignant melanoma. In that group, 13 patients were treated with chlorambucil-bound xenogeneic antimelanoma globulin (immunochemotherapy), and 11 received dimethyl triazenoimidazole carboxamide. Both patient groups were similar in age range, sex, tumor load and dissemination and performance status.

Of the 13 patients given immunochemotherapy, two showed objective responses, five had stabilization of their disease, and six showed tumor progression within three months of treatment; the median survival of the responders and stabilized patients was 20 months. None of the 11 patients responded to chemotherapy with dimethyl triazenoimidazole carboxamide, and all died within 11 months after beginning treatment; median survival was 3.5 months.

These investigators demonstrated that intravenous injections of chlorambucil-bound antitumor globulin is clinically feasible and can induce partial and even complete tumor regression in responders and in stabilized patients. The major limitation of such immunochemotherapy is sensitization to the antimelanoma globulin and the selective proliferation, after treatment, of drug-resistant tumor cells or tumor cells deficient in the surface antigen against which the xenogeneic antimelanoma globulin is directed.

Marital Status and Ovarian Cancer

Using data from the Third National Cancer Survey, 1969-1971, Weiss and associates (University of Washington and the Fred Hutchinson Cancer Research Center, Seattle, Washington) report that both black and white women over 25 years of age who had never married had a 60-70 percent higher incidence of ovarian cancer than in ever-married women. They analyzed 4,468 newly diagnosed patients entered on hospital and medical records and death certificates. Of the ovarian epithelial tumors, the clear cell and endometrioid types were more common in never-married women. The incidence of germ cell and sex cord-mesenchyme tumors showed no relationship to marital status. However, germ cell tumors tend to occur early in life, and thus marital status would not be expected to influence their etiology.