July

The search for additional genetic factors that may influence lung cancer is discussed in a guest editorial by Mulvihill (Clinical Epidemiology Branch, National Cancer Institute, Bethesda, Maryland). He terms this field "ecogenetics"—a word already used by geneticists to apply to the long-term effects of the environment on the genome—but he believes that it denotes a special use in medical genetics.

Cigarette smoking is the most important etiologic factor in bronchogenic carcinoma, and little evidence exists for genetic influences. However, certain characteristics of lung adenocarcinoma and alveolar cell carcinoma suggest familial factors unrelated to smoking. These neoplasms have been found in families with other tumors, acquired immune diseases or heritable disorders of the lung.

In the quest for additional genetic factors, the interaction of known environmental carcinogens with susceptible genotypes should be examined. The study of ecogenetics in oncology may bring about the development of a method for screening potential employees for abnormal genotypes that predispose them to neoplasia following occupational exposures that are harmless to normal genotypes.

Adamson and associates (Laboratory of Chemical Pharmacology, National Cancer Institute, Bethesda, Maryland) offer additional support for the hypothesis that humans exposed to aflatoxin B$_1$ (AFB$_1$) may be at risk for developing liver cancer. Field studies have suggested that AFB$_1$ is an important etiologic factor in the occurrence of liver cancer in inhabitants of some Asian and African countries.

Three rhesus monkeys, a species phylogenetically close to man, developed primary malignant neoplasms of the liver after being given AFB$_1$ plus dimethylsulfoxide (DMSO) for more than two years. No evidence of liver cancer was found in 20 control monkeys given DMSO alone. Liver biopsies of two of these monkeys showed pathologic lesions as early as one and four months after initiation of AFB$_1$ treatment. The serum alpha-fetoprotein level of one monkey with hepatic cell carcinoma paralleled tumor growth and recurrence. It is possible that serum alpha-fetoprotein levels will be useful in the detection of liver carcinoma and its regrowth after surgery.

August

Cancer treatment today and its impact on drug development are the subjects of a guest editorial by Carter (Division of Cancer Treatment, National Cancer Institute, Bethesda, Maryland). The Division of Cancer Treatment conducts clinical trials of new antitumor agents in three phases. Phase
I trials involve patients with tumors resistant to all currently available treatment. Determining the maximum tolerated dose and parameters of toxicity are among its aims. In Phase II, new drugs are screened for clinical antitumor activity worth further testing. The ultimate value or role of a given drug is the purpose of the large-scale Phase III studies. The Phase II trial of a new drug is only one of many options available today to persons with advanced disease. Combination chemotherapy is so successful that the question of ethics in testing a new drug in patients not previously treated by chemotherapy might be raised.

Some major changes in cancer therapy that have had significant impact on drug development include the discovery of many active drugs, the widespread application of combination chemotherapy, combined modality approach with long-term adjuvant chemotherapy and the rise of immunology and immunotherapy. These changes have raised questions about future development, the search for new drugs and criteria for selection for clinical trial. Another aspect of drug development which merits consideration is the long-range possibility that, as the control of cancer is increased, the role of chemotherapy in advanced disease will be diminished. Since advanced disseminated disease will no longer be commonplace, the classic "testing grounds" will shrink. Thus, if drug development is successful, "it will put itself out of business."

Dr. Carter discusses in detail the results of clinical trials of drugs on cancer of the breast, ovary, uterus, genitourinary tract, large bowel, stomach, pancreas, lung, head and neck and central nervous system as well as malignant melanoma and lymphoma and the leukemias.

Waalkes et al. (Division of Cancer Treatment, National Cancer Institute, Bethesda, Maryland) measured the urinary levels of \( \beta \)-aminoisobutyric acid (\( \beta \)-AIBA), \( \beta \)-alanine and other normally excreted \( \alpha \)-amino acids of five patients with Burkitt's lymphoma before, during and after chemotherapy. The patients were children four to 12 years old, who were admitted to the Pediatric Oncology Service at NCI. All except one had greatly elevated urinary levels of \( \beta \)-AIBA and normal levels of \( \beta \)-alanine before treatment. After four to eight days of chemotherapy, the \( \beta \)-AIBA levels fell in accordance with clinical evidence of tumor destruction, and \( \beta \)-alanine levels were normal. In six to 12 months, when two of the patients were considered free of disease, the levels of the two \( \beta \)-amino acids were within normal limits.

Further studies may determine whether the abnormal excretion of \( \beta \)-AIBA may be an important measure in the estimation of disease status of patients with Burkitt's lymphoma and similar neoplastic diseases.