SECOND EDITION

Cancer Medicine

JAMES F. HOLLAND, M.D.

Professor and Chairman
Department of Neoplastic Diseases
Professor of Medicine and Chief
Division of Medical Oncology
American Cancer Society Professor of Oncology and Director, The Cancer Center
Mount Sinai School of Medicine of the City University of New York
New York, New York

EMIL FREI III, M.D.

Professor of Medicine
Harvard Medical School
Director and Physician-in-Chief
Sidney Farber Cancer Institute
Boston, Massachusetts

In collaboration with 184 contributors

LEA & FEBIGER • *1982* • PHILADELPHIA

XX-3

Acute Myelocytic Leukemia

ROSE RUTH ELLISON

Acute myelocytic leukemia (AML) is a heterogeneous disease or group of diseases occurring primarily in adults, characterized by replacement of normal marrow elements by immature cells of tne myeloid series. Whether this abnormality in differentiation results from an imbalance of inhibitory and stimulatory factors and is potentially reversible or whether it represents an intrinsic and irreversible malignancy of these cells independent of their ability to mature is still unsettled.

Etiology

A number of factors-have been incriminated in the causation of acute and chronic myelocytic leukemia (CML).[1-10] These include x-irradiation, exposure to certain chemicals, genetic and congenital factors, and perhaps viral infections.

Radiation Exposure. Acute leukemia (predominantly but not exclusively myelocytic) and chronic myelocytic leukemia (CML) have been known to follow radiation exposure. Radiologists, prior to the development of modern safety techniques, had an increased incidence of myelocytic leukemia. A dose-dependent increased frequency of acute and chronic myelocytic leukemia was observed in patients with ankylosing spondylitis treated with radiotherapy.

The most striking data concerning the role of irradiation in the production of leukemia are those obtained in the survivors of the 1945 atomic blasts at Hiroshima and Nagasaki. These events were followed by an increased incidence of both CML and AML the increase continued for nearly 20 years after exposure. Thus, in 1964 the incidence of AML for those less than 1500 meters from the hypocenter was still significantly greater than for individuals who were at a greater distance. The incidence of acute leukemia occurred in a bimodal fashion, with peaks in 1951 and 1958. The dose-induced relationships for total body irradiation suggested a lack of leukemogenic effect at dose levels below 50 rads, but the existence of a threshold level has not been proved. An increased risk for males over females was seen.

A retrospective study concluded that approximately 3% of all AML and CML were possibly induced by therapeutic radiation. with doses of the same order as those leading to leukemia in Hiroshima, and after treatment for spondylitis.[5-7] These authors did not find a relationship between diagnostic irradiation and development of leukemia. Another retrospective review of diagnostic radiation exposure did indicate a significant increase in AML and CML for men (but not in women),[79] with the increased risk related to the number of films taken; the risks in men were greater for those who had diagnostic radiation of the trunk. There was no increase in acute lymphocytic leukemia.

Chemical Exposure. The drugs implicated as leukemogens are all known to cause bone marrow depression and/or aplasia. The only compound with an unequivocal relationship to AML is benzol.[3] Exposure to benzol, sometimes seemingly trivial, has been followed by the development of AML with or without the clinically recognized intermediate steps of aplastic anemia, other cytopenias, myelofibrosis, or myeloid metaplasia. Other putative leukemogens include chloramphenicol,[42,156] phenylbutazone,[12] and perhaps arsenicals, sulfonamides, and various insecticides.

Treatment of multiple myeloma with phenylalanine mustard or cyclophosphamide with or without irradiation has been followed by the occurrence of AML,[109,193] although this complication has been seen rarely without *history* of exposure to either mode of therapy.

AML has also followed chronic use of alkylating agents in the treatment of other neoplastic diseases, including ovarian cancer, gastric cancer, and Hodgkin's disease. Acute myelocytic leukemia has been diagnosed 1 to 20 years after initiation of treatment in Hodgkin's disease.[194] It has been seen in patients who have received intensive radiotherapy alone or chemotherapy alone, but has been particularly noted in patients who received both intensive radiation therapy and chemotherapy