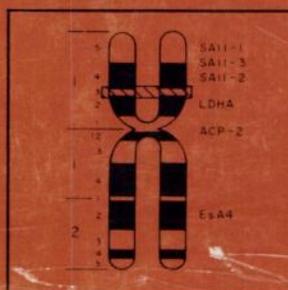
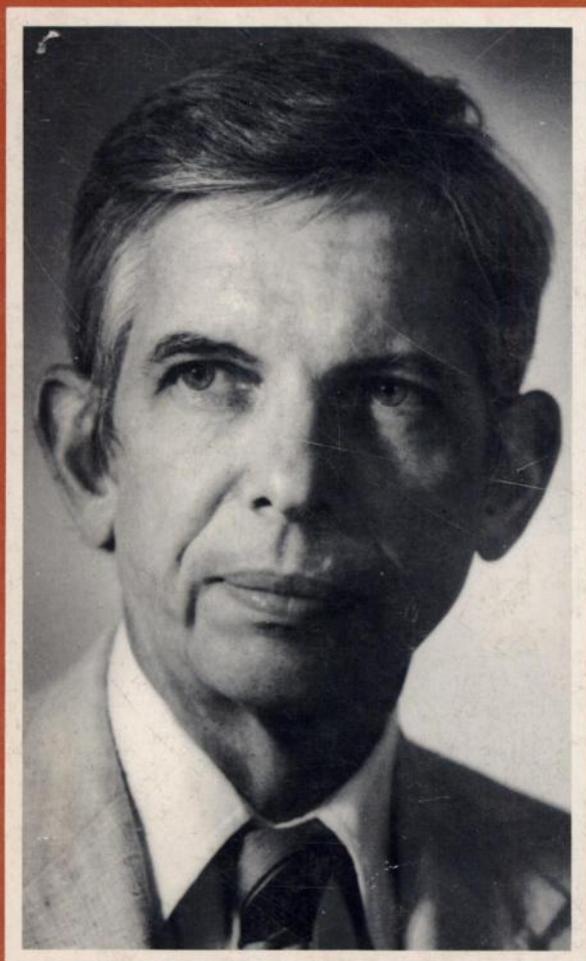


Cancer Research

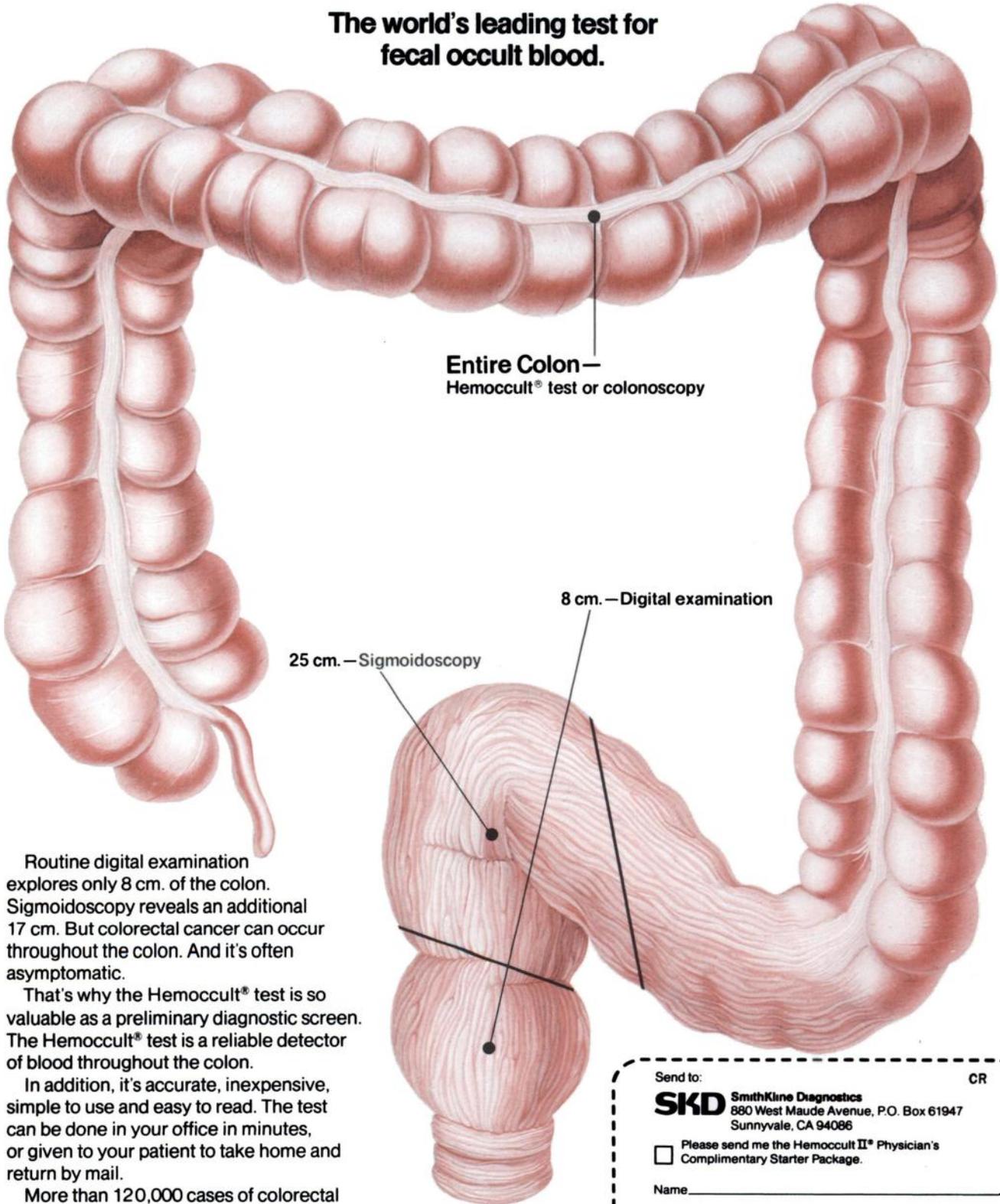
VOLUME 41 • NO. 5 CNREA 8 • PP 1579-2023

May 1981



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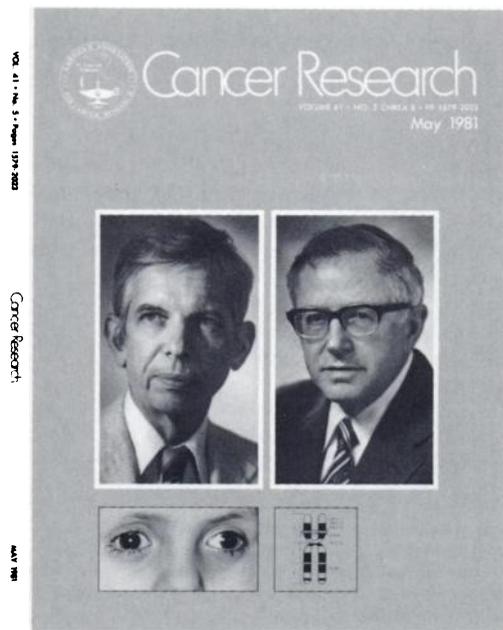
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COVER LEGEND



In the early 1960s, the epidemiology-etiology of childhood cancer other than leukemia was unexplored. Data by cell type were generally not available from death certificates on which cancers were coded by anatomical location. In consequence, for example, Ewing's tumor and osteosarcoma were merged under a single code number for malignant bone tumors in the International Classification of Diseases.

Through the use of medical records in multihospital series and by recoding about 40,000 diagnoses on death certificates for children who died of cancer in the United States in the 1960s, Robert W. Miller, M.D., Chief of the Clinical Epidemiology Branch, and associates at the National Cancer Institute showed dynamic changes in mortality by single year of age for certain cancers, a gradual rise with age of other neoplasms, the near absence of Ewing's sarcoma in blacks, the types of cancer diagnosed at birth or soon thereafter (indicative of intrauterine origin), the occurrence of certain malformations with specific cancers (e.g., Wilms' tumor and aniridia, now known to be related to deletion of a portion of the short arm of chromosome 11, as shown on the cover), the increased risk of certain cancers in siblings and families, and their similarity to the types of cancer that occur as second primaries in individual patients (N. Engl. J.

Med., 268: 393-401, 1963; 270: 922-927, 1964; 271: 30-36, 1964; 275: 87-93, 1966; and 285: 307-311, 1971). From such gross observations on human disorders for which no animal models were known, new perceptions of cancer biology could be made by laboratory investigators.

Alfred G. Knudson, Jr., Ph.D., New Director of the Institute for Cancer Research, Fox Chase Cancer Center, Philadelphia, synthesized this and other information concerning several childhood tumors (retinoblastoma and, with Louise C. Strong, Wilms' tumor and neuroblastoma) to show that, when these neoplasms were multifocal and/or familial, the age at diagnosis was generally earlier than in sporadic, non-familial cases (Proc. Natl. Acad. Sci., U.S.A., 68: 820-823, 1971; J. Natl. Cancer Inst., 48: 312-324, 1972; and Am. J. Hum. Genet., 24: 514-532, 1972). The differences in the shapes of the graphs for the two classes of tumors (*i.e.*, hereditary-multifocal versus sporadic-unifocal) suggested that one postzygotic event was involved in the former, two in the latter. In the hereditary cases, the first event was a germinal mutation that affected all target cells, and the second was a postzygotic event which produced transformation, often at more than one site. In the nonhereditary cases, both events were postzygotic which by rare chance would affect the same cell, thus accounting for the unifocal nature of the tumors in these patients. Subsequent observations by other investigators support the hypothesis, as for example the discovery by Bove and McAdams that in bilateral Wilms' tumor subcapsular renal dysplasia is consistently found. These lesions presumably represent an effect of the germinal mutation, which a second (postzygotic) event may transform into a malignant tumor. Knudson and Strong also showed that Wilms' tumor associated with aniridia behaved like the hereditary form of that tumor and noted that a chromosomal deletion could account for the association. Patients with the deletion (shown by Riccardi to be at 11p13) may have aniridia without Wilms' tumor, further indicating that a second event is involved in the genesis of this tumor.

Dr. Miller (*right*), b. 1921, received his medical training at the University of Pennsylvania and a doctoral degree in epidemiology at the University of Michigan. Dr. Knudson (*left*), b. 1922, received his medical training at Columbia University and a doctorate in biochemistry and genetics at the California Institute of Technology. Both were trained in pediatrics.

Breast Cancer Research and Treatment

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AIMS AND SCOPE

Breast Cancer Research and Treatment provides the surgeon, radiotherapist, medical oncologist, endocrinologist, epidemiologist, immunologist or cell biologist investigating problems in breast cancer a single forum for communication. The journal creates a "market place" for breast cancer topics which cuts across all the usual lines of disciplines, providing a site for presenting pertinent investigations and for discussing critical questions relevant to the entire field. It will help to develop a new focus and new perspectives for all those concerned with breast cancer.

Volume 1, 1981, will be published in four issues. Each issue will contain approximately 4 articles dealing with original laboratory investigations and 4 articles dealing with clinical studies. There will be sections devoted to invited review articles, pro and con discussions of controversial subjects, editorials, and reports from organizations such as the US-Breast Cancer Task Force, EORTC, and NSABP. There will be a section for letters to the editor, which should provide for a lively exchange of opinions on previously published articles or other topics of interest. There will also be an opportunity to publish the proceedings of special workshops, symposia, etc, devoted to breast cancer. All manuscripts will be peer reviewed by a distinguished group of advisory editors from various disciplines of breast cancer.

SUBSCRIPTION RATES

The subscription price for 1981, Volume 1 (4 issues) is: For institutions Dfl. 130.00/US\$ 68.50 plus Dfl. 21.00/US\$ 11.00 for postage and handling. For individuals Dfl. 85.00/US\$ 45.00 including postage and handling. For airmail delivery please add Dfl. 18.00/US\$ 9.50. The journal is shipped to the USA and Canada in bulk airfreight at no extra cost. For SAL (Surface-mail Air Lifted) shipment to Australia, India and Japan please add Dfl. 10.50/US\$ 5.50.

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