The National Cancer Institute
Cooperative Clinical Trials Program

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The Division of Cancer Treatment (DCT) of the NCI allocates funds for a large cooperative clinical trials program to evaluate different therapies for cancer. This program currently involves 558 domestic and foreign institutions, over 4,000 investigators, and some 60,000 patients who are on active treatment studies or in follow-up. It is the largest clinical treatment evaluation program in medicine. Since physicians not directly involved with the program may find its complexities confusing, we believe it is useful to provide an overview of the organization and scope of these cooperative groups.

The cooperative group concept was initiated in 1955 by the NCI because of the need to clinically test the new anticancer drugs being studied in the NCI animal drug screening program. At that time there were few drugs available for the treatment of cancer; there were even fewer physicians interested in treating cancer patients with these new drugs. One of the cancers for which several drugs had proven of some value was fairly uncommon—acute lymphocytic leukemia (ALL). No single institution had an adequate number of patients to sufficiently test and, consequently, the NCI staff encouraged the formation of groups of institutions and investigators to conduct cooperative studies of cancer treatment. There were originally only three groups: Acute Leukemia Group A, Acute Leukemia Group B, and the Eastern Solid Tumor Group. The first two were assigned the task of studying purine antagonists and methotrexate in the management of childhood ALL; the Eastern Group evaluated nitrogen mustard and thioTEPA for the carcinomas. Each of these groups consisted of a handful of investigators and institutions. Twenty-five years after this modest beginning, the initial three groups have increased to 13, and the number of active studies has grown to over 400, encompassing most adult and childhood cancers. Table 1 lists the groups currently active and their respective group chairmen. Also listed are the diseases with intergroup studies and the projects that provide scientific support to the groups.

Whereas the first group members were pediatricians, internists, and pharmacologists, today all specialties involved in oncology are represented: general surgery and the surgical subspecialties; medical oncology; radiation oncology; pediatrics; pathology; psychiatry; immunology; and oncology nursing. Each group is also

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staffed by or affiliated with statisticians experienced in clinical trials who help design studies and perform data analysis. When a study is completed, these statisticians help prepare the final reports for dissemination through the customary scientific channels.

Although the original mission of the cooperative groups was to test the cancer drugs available in 1955, the scope of their work has expanded to include new drug testing, multimodal treatment comparative trials, comparative testing of various types of cancer surgery, adjuvant drug treatment after cancer surgery, and the analysis of psychological changes as a result of cancer treatment. Studies may also involve comparisons of histology and treatment response, stage and response, and radiotherapy techniques and radiation sources, in addition to the testing of innovative treatment approaches that may be more advantageous than current methods. Most studies are randomized, comparing two or more treatments. Frequently, one of the treatments being compared is the best "standard" treatment; this serves as a control. When patient accrual allows, some studies may involve as many as six or eight simultaneously compared treatment regimens.

Each group meets semiannually to review current results and to formulate further studies. In this way a constant

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TABLE 1

| DCT Cooperative Clinical Trials Program | Chairman |
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| MULTIMODALITY MULTIDISEASE GROUPS       |          |
| Cancer and Leukemia Group B (CALGB), Scarsdale, NY | James F. Holland, M.D. |
| Children's Cancer Study Group (CCSG), Los Angeles, CA | Denman G. Hammond, M.D. |
| Eastern Cooperative Oncology Group (ECOG), Madison, WI | Paul P. Carbone, M.D. |
| Northern California Oncology Group (NCOG), Palo Alto, CA | Stephen K. Carter, M.D. |
| Southeast Cancer Study Group (SEG), Birmingham, AL | John R. Durant, M.D. |
| Southwest Oncology Study Group (SWOG), Kansas City, KS | Barth Hoogstraten, M.D. |
| MULTIMODALITY SINGLE AREA OF DISEASE GROUPS |          |
| Gynecological Oncology Group (GOG), Philadelphia, PA | George C. Lewis, M.D. |
| National Surgical Adjuvant Breast and Bowel Project (NSABP), Pittsburgh, PA | Bernard Fisher, M.D. |
| National Wilms' Tumor Study Group (NWTSG), Philadelphia, PA | Julio D'Angio, M.D. |
| Polycythemia Vera Study Group (PVSG), New York, NY | Louis R. Wasserman, M.D. |
| Veterans Administration Surgical Oncology Group (VASOG), Washington, DC | George A. Higgins, M.D. |
internal review of the performance of a group and its membership is maintained. Most groups have minimum standards of yearly patient accrual and evaluality and scientific input that institutions must meet to retain group membership. The performance of each institution and its principal investigator is also reviewed by both the scientific peer review system and the NCI staff at the time of grant renewal.

Studies originate from group members and modifications are made in a process of extensive review of each study within the group membership. The NCI helps coordinate the work by assigning staff members to attend group meetings and by providing liaison with the group chairmen and their administrative personnel. Proposed protocols are reviewed at the NCI and revisions may be suggested. Informal working conferences are held periodically in Bethesda to review the current status of treatment in a par-

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ticular cancer and to help develop new directions for investigation. Interested group members and disease committee chairmen participate in these conferences. Similar small working conferences are held by the groups also.

Since their formation, the cooperative groups have been involved in most of the progress made in the management of cancer. They have either initiated and documented the value of a new concept themselves or have provided the means to validate in a large number of patients the results of single institution initiatives. A large portion of the new anticancer drugs have been tested and validated in group studies. Ancillary programs, such as those designed to define tumor responses and standardize cancer treatment evaluations, have been fundamental to the groups' efforts and contributions. Most of the major clinical trials that have proven that the administration of chemotherapy after resection of the primary lesion is beneficial for some tumors have been conducted by the groups.

In addition to grant funds from the DCT, several of the groups receive funds from the Division of Cancer Control and Rehabilitation to assist with their activities in making available the best cancer care for community hospitals. Many non-university hospitals collaborate with the groups' major institutions to test new treatments and to provide the most up-to-date medical care for cancer patients. A by-product of these activities is the exposure of medical students, house staff, and primary care physicians to the tenets of cancer medicine.

The cooperative group system has evolved to meet new demands and changing concepts. A number of groups have been formed and disbanded since 1955 as needs have changed or as a group's work failed to pass scientific peer review. The cooperative groups—changing to meet changing needs—will remain a vital segment of cancer treatment investigation with research initiated by the investigators and coordination of activities by NCI staff.

MODERN HAZARDS, ANCIENT TASK

It is good that man must work in order to live. But work can also be harmful, and the development of industry created a vast array of new hazards that threatened not only the worker's health and life but also that of society at large. Industry has brought man very close to physical and chemical forces of tremendous potency. It has become the physician's duty to protect him against these new hazards and the task is one of such magnitude that the co-operation of scientists and engineers is required.

Sigerist HE: Medicine and Human Welfare. College Park, Maryland, McGrath Publishing Company, 1970, p 131.