THE CANCER LETTER

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TREATMENT PROGRESS SINCE 1972 PROVIDES POWERFUL SUPPORT FOR CONTINUING NATIONAL CANCER PROGRAM

The staff of Sen. Edward Kennedy's Health Subcommittee submitted a list of questions to NCI, to be answered at the subcommittee's oversight hearings on the National Cancer Program. Question No. 6 was one which NCI executives, especially Div. of Cancer Treatment Director Vincent DeVita, were more than eager to answer:

"Please describe the major clinical advances in the treatment of cancer since the passage of the National Cancer Act. for each such advance, please identify the investigators most directly responsible for the advance, the citation or citations identifying the initial publication of that advance, whether or not the National Cancer Institute funded the work which led to that advance, and if so, the extent of Cancer Institute support. For each such advance, please specify whether the Cancer

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In Brief

ROGERS ON AHF BOARD; GAO SAYS LEGISLATION MAY BE NEEDED FOR HOSPICE REIMBURSEMENT

PAUL ROGERS, former chairman of the House Health Subcommittee who retired from Congress last year, has been elected to the Board of Trustees of the American Health Foundation. Rogers is now with the D.C. law firm of Hogan & Hartson. . . . **GAO REPORT** on hospice care, summarizing a study requested by Sens. Ribicoff, Kennedy and Dole, offered no recommendations other than that laws governing Medicare, Medicaid, Social Services and Older Americans programs may have to be amended to cover all services hospices provide. The report noted there is no standard definition of a hospice or of what services an organization must provide to be considered a hospice; 59 organizations in the U.S. consider themselves to be hospices; 73 others plan to establish hospice care programs; the four programs named above can pay for at least some services provided by hospices. Single copies of the report (HRD 79-50—"Hospice Care—A Growing Concept in the U.S.") may be obtained free from U.S. General Accounting Office, Distribution Section Rm 1518, 441 G St. N.W., Washington D.C. 20548. . . . **MARVIN RICH**, executive vice president and scientific director of the Michigan Cancer Foundation and deputy director of the Comprehensive Cancer Center of Metropolitan Detroit, has been elected to the Board of Directors of the Assn. of American Cancer Institutes. . . . **HODGKIN'S, NON-HODGKIN'S** lymphomas—epidemiology, diagnostic and treatment methods, with emphasis on nursing implications and responsibilities will be included in the program of the third annual Regional Nurses Conference June 14-15 in Wilmington, Del. The conference is open to all nurses and supportive health care professionals. Contact Joanne Tully Cossman, Delaware Cancer Network, 1202 Jefferson St., Wilmington 19801, 302-428-2112.

NCI DESCRIBES PROGRESS IN TREATMENT, NEW DRUGS, RADIOTHERAPY, SURGERY

(Continued from page 1)

Institute supported (a) the research which made the advance possible, (b) the refinement or development of the advance, or (c) the dissemination of the advance."

NCI compiled a 51-page answer to that question. Although DeVita did not have the opportunity to present it verbally at the hearing, it will be included in the permanent record. It completely demolishes the positions of critics who have been contending that there has been no progress in treating cancer patients. It should provide a powerful argument for renewal of the National Cancer Act next year.

The statement summarizes progress in treating 16 types of cancer, development of major new anticancer drugs, and progress in radiotherapy, surgery, immunotherapy and other treatment areas. Excerpts follow:

According to the End Results Report No. 5 of NCI, 41% of all patients with cancer can be expected to survive five years without evidence of disease. This is in contrast to a survival rate of 20% in 1930 and about 33% in 1955. The earlier increases in survival were brought about primarily through improved surgical and radiotherapeutic techniques. Much of the improvement in survival since 1955 has resulted from new and improved approaches to chemotherapy and the Drug Development Program begun at that time. Representative of highly significant improvements are the chemotherapeutic management of advanced Hodgkin's disease and acute childhood leukemia.

In order to place these numbers in perspective, it is worthwhile reviewing the total incidence of cancer. In 1977 there were 700,000 new cases of cancer, exclusive of skin and in situ cervical cancer. These two cancers are excluded because they are now rarely lethal (99% curable). If one adds skin cancer and in situ cervical cancer to the list, the total incidence is more than a million new cases of cancer diagnosed each year in the United States.

Five hundred thousand of the 700,000 patients with cancer have disease that can be operated on and/or treated with radiotherapy as the initial treatment. Two hundred thousand of the 700,000 patients, however, exhibit metastatic disease at the time of initial diagnosis. Ninety-two thousand of the 200,000 patients can be expected to benefit from existing chemotherapy. Sixty thousand of the 92,000 can expect to have their lives prolonged by existing chemotherapy.

At present there are 11 malignant diseases in which cures have been obtained. The incidence of these 11 diseases each year is approximately 46,000. Approximately 32,000 or 70% of these patients are diagnosed with metastatic disease. Eleven thousand of these 32,000 patients with widespread tumor can be expected to be cured with existing chemotherapy and the remaining 21,000 patients have a significant prolongation of useful life. These tumors have served as the theoretical basis for drug treatment of the more common types of cancer of adults. It is interesting to note that national mortality of patients who are affected by these tumors has decreased as a result of the widespread application of these treatments. For example, the mortality from Hodgkin's disease has decreased 30% in the last five-year reporting period. Many of these diseases occur in children or young adults. It can be estimated that half of all patients below the age of 15, who develop cancer, can now expect to be rendered free of their disease with followup periods as long as 15 years. Though decreasing mortality data are not at present as striking in all tumors as that with Hodgkin's disease and acut lymphocytic leukemia of childhood, this is likely due to the recent development of many of these treatments and the shorter followup time.

In recent years we have been examining ways to alter the fate of the 500,000 patients who present with operable cancer per year.

This amounts to 71% of all patients with cancer. While approximately 280,000 of these 500,000 patients can be expected to remain free of tumor with either surgery or radiotherapy alone, it is important to consider that 220,000 of the 500,000 patients can be expected to develop recurrence—because of apparent microscopic foci. Major emphasis has been placed on the development of effective therapies for this population since the establishment of the National Cancer Program.

In many cases, these therapies have utilized a combined modality approach to this difficult problem of recurrent cancer. Emphasis has been placed on giving additional treatment, usually chemotherapy, once the local therapy has been given to patients who are known to have a high risk for recurrence. One hundred fifty thousand of the 220,000 patients mentioned above are considered prime candidates for postoperative drug treatment. They are considered prime candidates because existing drugs are known to be effective against the disease even when it is in its advanced stage. These diseases are: breast, ovarian, bladder, colon and head and neck cancers. Since chemotherapy has been effective under the most adverse circumstances on patients with metastatic disease, it is reasonable to expect that chemotherapy will exert an even greater impact on the survival of patients treated in the postoperative period under more ideal circumstances.

In summary, it is clear that chemotherapy is contributing significantly to the survival of cancer patients. As new active drugs and drug combinations emerge and are incorporated into combined modality regimens, we should begin to observe improved survival in many of the other common tumors as we

have already observed in breast cancer and hope to observe in colon cancer.

Breast Cancer

Therapy for breast cancer has been one of the areas where significant progress has been accomplished in the 1970s. Much of the foundation for these advances was laid in the 1960s with the development of effective combination chemotherapy for advanced disease by Cooper (Univ. of Rochester) and the intramural NCI program. These and other confirmatory trials demonstrated that combination drug therapy can significantly prolong the lives of those women who respond. These clinical trials coupled with preclinical work carried out by Martin paved the way for one of the most dramatic advances in the treatment of this disease.

Two clinical trials were initiated in 1972 to test the value of chemotherapy given after mastectomy to patients identified to be at high risk of recurrence. Both groups, the National Surgical Adjuvant Breast Project and the Institute Nazionale Tumori, Milan, have shown a significant improvement in disease-free survival for the treated premenopausal patients. In the Milan study, a highly significant improvement in survival at four years for the premenopausal group of women has been noted, rising from 71% to 90%. Even more impressive is that in the highest risk group of patients, those with greater than three lymph glands involved with tumor, an improvement in relapse-free survival from 23 to 51% has been noted. We expect that this improvement in survival should be translated into a detectable national decrease in mortality from breast cancer in women under the age of 50 in the U.S. by the early 1980s.

Reducing the morbidity from breast surgery is also an important goal. Prior to 1971, the Halsted radical mastectomy and modified radical had become the standard operations in the primary treatment of breast cancer. During the past decade the NSABP has addressed itself to whether such extensive surgery is necessary. From results of surgical studies initiated in 1972, it is possible to state that radical mastectomy is no more effective than the less deforming procedures. The NSABP currently is studying the efficacy of segmental mastectomy (lumpectomy). Evaluation of these trials will await further followup.

A whole new area of scientific understanding of breast cancer and hormone responsiveness has developed during the 1970s. The identification of estrogen-binding proteins by Jensen in the late 1960s was followed by data supporting the use of the presence of receptors in breast cancer tissue to predict clinical responsiveness of the patient to hormonal manipulation. Recent work in the NCI intramural program demonstrated that the receptor-negative patients are more responsive to chemotherapy. These advances thus hold the possibility of further scientifically individualizing patient therapy. Extent of NCI funding for research cited: $10,840,000, 1972-1978.

Osteosarcoma

In the past, this malignant bone tumor was curable in only 20% of patients subjected to amputation. Recent use of adjuvant chemotherapy has increased the disease-free survival to 60% at five years. In addition, aggressive pursuit and resection of pulmonary metastases has further increased the survival of those patients who relapse so that the overall cure rate in some studies is now estimated to be 70%.

These advances are attributed to the efforts of several institutions and clinical cooperative groups, all funded by grants or contracts from NCI. Extent of NCI funding for research cited: $3,551,000, 1972-1978.

Non-Seminomatous Testicular Cancer

Between 1960 and 1970, chemotherapy of advanced testicular tumors provided a high rate of short term regressions but failed to yield significant improvement in long term complete remissions, which averaged less than 10%. The last few years have witnessed the development of combinations of active chemotherapeutic regimens capable of inducing complete remission status in 80% of all patients treated. Furthermore, 50% of all treated patients now should now be curable.

The pivotal clinical trials leading to this advance were by Samuels, Golbey et al., and Einhorn and Donodue. These combination chemotherapeutic approaches, combined with the development of tests for measuring small amounts of residual tumor tissue, have led to the recent initiation of trials in the patients with earlier stages of disease in which we might well expect 100% curability rates.

Funding for the studies completed at M.D. Anderson and Memorial Sloan-Kettering have been solely from NCI. NCI supplied investigational drugs to Einhorn and Donohue at Indiana Univ. for their clinical trial. Extent of NCI funding for research cited: $606,000, 1976-1978.

Pediatric Malignancies

Half of all children with cancer should now remain disease-free with current therapy.

Acute Lymphatic Leukemia: The early work in acute leukemia therapy which preceeded the passage of the National Cancer Act, has been refined since 1971. The major advances in this disease since then is that we have learned that greater than 80% of children with the null cell variety of acute lymphatic leukemia are curable. This information awaited development of tests since 1971 to identify the cell of origin of lymphocytes. The remainder of patients with ALL form the higher risk group under intensive study. Efforts are now being made to refine the treatment of null cell leukemia to make it less toxic while retaining the high cure rate.

Wilm's Tumor: By 1971 40% of patients with Wilm's tumor were curable with surgery and X-irradiation. Since then it has been demonstrated that 90% of children can be cured using drugs, X-irradiation

and surgery together. An important recent finding is that a two-drug combination with surgery yields the same results. The omission of radiotherapy reduces the morbidity of this treatment and results in less loss of growth potential for these children who can expect a long life span.

Rhabdomyosarcoma and Ewing's Sarcoma: These common childhood tumors of connective tissue and bone were once cured in only 10-20% of cases. From data developed since 1972, we now know it is possible to cure 60-70% of these patients. These dramatic results are attributable to two major advances: 1) the demonstration that combination chemotherapy will eradicate metastatic cancer and 2) the demonstration that combined modality therapy—surgical resection, radiation of the tumor bed, and chemotherapy for distant tumor spread, is a curative treatment strategy.

These studies in cancer centers and cooperative groups were funded by grants from NCI. Eighty percent of funds were spent for the conduct of clinical trials and 20% for developmental work in surgery, radiation, and chemotherapy. NCI funding: $2,757,000, 1972-1978.

Small Cell and Epidermoid Carcinoma of the Lung

It is estimated that approximately 20,000 adults will develop small cell carcinoma of the lung each year. Prior to 1972, no effective therapy was available for this devastating disease (median survival of most patients from diagnosis was two months). With appropriately administered chemotherapy, and in some cases radiation therapy, the median survival has increased to approximately one year with 25% of the successfully treated patients living longer than two years. Development and refinement of these treatments took place in cooperative group studies. NCI funding, $5,784,000, 1975-1978.

Adult Acute Leukemia

Untreated adult leukemia is a rapidly fatal disease. The remission rate was about 20% in the 1960s and editorials appeared in the medical literature suggesting that treatment was not beneficial to most patients. In that decade, few patients lived beyond six months and most died within weeks of diagnosis.

Daunorubicin was shown to produce complete remissions in 40% of patients in 1972. This intramural NCI work was confirmed and extended by a large cooperative group trial. Cytosine arabinoside was thoroughly investigated in the late 1960s at M.D. Anderson and found to produce a 25% complete remission rate. This work was later confirmed by another large cooperative group trial.

A pilot study demonstrated in 1972 that the combination of these two drugs was more effective than either drug alone. Again, a large cooperative group study confirmed the observation from the pilot study that the two drugs in combination produced a 65% complete remission rate. These treatment advances are measured in terms of improved survival. There were virtually no long-term survivors of this disease in 1967 whereas a 12.5% survival of more than four years has recently been reported.

Since the National Cancer Act, complete remission rate and median survival has doubled in adult acute leukemia and a fraction of long term disease free survivors has emerged. NCI funding, $5,775,000, 1972-1978.

Soft Tissue Sarcoma

Prior to 1972, there was no effective therapy for disseminated soft tissue sarcoma when the disease recurred after primary surgery or presented in its advanced state. The identification of effectiveness of adriamycin against this tumor by Gottlieb and coworkers and the later studies of Bonadonna utilizing DTIC, an NCI-developed drug, provided a foundation to build further effective combinations of chemotherapy treatments. Response rates for many drug combinations are now in excess of 50% and remission duration and survival have improved commensurately.

In the past radical surgery was the major form of primary treatment of soft tissue sarcomas in adults but recurrence rates following surgery were high. During the past five years, further studies have been initiated to test the addition of chemotherapy to the initial surgical procedure. The results of these studies indicate a marked decrease in recurrences and represent a major breakthrough in the management of those diseases.

These studies have subsequently led to trials utilizing limb-sparing procedures combined with radiation and chemotherapy. Results indicate this innovative approach achieves cure rates equivalent to radical surgery alone when also followed by chemotherapy. Projected survival in these studies will far exceed the 39% five-year survival from various surgical series published in the 1960s. These data offer the exciting prospect of effective yet less morbid treatment for these children and young adults. NCI funding, $2,922,000, 1972-1978.

Hodgkin's Disease

Treatment results in this disease have been dramatically improved in the past decade. Approximately 70% of all patients presenting with this tumor will achieve a normal life span with treatment consisting of radiotherapy, chemotherapy or both used together.

The most significant advance contributing to this improvement prior to 1972 was the development of effective combination chemotherapy for this disease, namely the MOPP program (nitrogen mustard, vincristine, procarbazine and prednisone). This regimen was developed at the Medicine Branch of NCI. In patients with advanced stage III and IV disease MOPP raised the complete response rate from 20% to 81%. Before MOPP chemotherapy the median survival of these patients was two years or less. In patients who achieved remission MOPP produced an 82% survival at five years and 72% at 10 years. These results were confirmed in a subsequent study.

Since then the search for a drug combination with

efficacy in patients failing MOPP therapy yielded a new regimen consisting of adriamycin, bleomycin, vinblastine and DTIC (ABVD) reported by Bonadonna et al in 1975. ABVD produced complete remissions as frequently as MOPP and positive effect in MOPP failures was demonstrated. A subsequent study showed a 61% complete response rate to ABVD in patients who failed MOPP.

ABVD has now been combined with MOPP (in alternating monthly cycles) to treat advanced Hodgkin's disease by Bonadonna, again with NCI support. This regimen produced a higher percentage of complete responders and longer duration of those responses. If these trends continue, this combined regimen will be a significant improvement to the MOPP program.

Since 1971 a brilliant series of clinical studies has been in progress at Stanford Univ. determining the relative value of MOPP and varying amounts of radiotherapy in patients with early stages of Hodgkin's disease. Results so far indicate a marked improvement in survival in all stages. In some stages of Hodgkin's disease treated with Stanford methods there have been no deaths from the disease for over five years. Newer trials are attempting to achieve the same results with less morbidity by gradually reducing the amount and extent of radiation therapy. This work has been supported entirely by NCI. Funding, $5,390,000, 1972-1978.

Non-Hodgkin's Lymphoma

Since 1971 studies have shown that the majority of adults with advanced stages of the non-Hodgkin's lymphoma of the diffuse histiocytic variety are curable with the use of newly developed combination chemotherapy. These clinical studies were initially reported from the intramural program of NCI, and subsequently refined and developed in the clinical cooperative groups under NCI support.

These drug programs have subsequently been tested in adjuvant treatment of patients with early stage tumors, to prevent recurrences outside radiation treatment fields. Bonadonna and colleagues have recently reported positive results in their adjuvant trial.

The pediatric non-Hodgkin's lymphomas are a diverse group of neoplasms, but are substantially different from those in adults, with a more frequent abdominal presentation and more frequent transition to acute leukemia. Several recent advances have been made. Complete resection and postoperative radiotherapy are now producing 70-80% cures in patients with limited abdominal disease.

Pediatric mediastinal lymphoma is an aggressive disease of male adolescents which almost universally terminates in a refractory leukemia. Treatment results in the 1960s were dismal, with virtually no long term survivors. Recently, poly drug chemotherapy developed at Memorial Sloan-Kettering has resulted in an 88% three year survival, vastly improving the prognosis in these patients.

Pediatric lymphomas localized to the head and neck have been recently reported to have a 52% long term survival rate when treated by radiation therapy plus chemotherapy. This also represents a significant advance over earlier results with radiation alone. NCI funding, $4,539,000, 1972-1978.

Ovarian Cancer

This is the fourth most frequently diagnosed cancer in American women and is the most common fatal gynecologic malignancy. Recent advances have led to hopes that significant improvement will be made in decreasing these mortality statistics.

The chemotherapy of advanced ovarian cancer has undergone a number of changes in the past five years. Only the single agent L-PAM was available to treat patients with widespread ovarian cancer prior to 1971. The effectiveness of the new agents, adriamycin, hexamethylmelamine and cis-platinum has been identified since then as a result of the NCI drug development and clinical trials programs. When these drugs are used in combination, improved results have been obtained. In an NCI controlled clinical trial studying the chemotherapy of advanced ovarian cancer, the results show an improvement in survival for patients treated with a combination of drugs as compared to those treated with L-PAM. NCI is supporting an ovarian cancer study group where the use of chemotherapy and radiotherapy is being studied in patients with early stages of ovarian cancer who have a high risk of developing recurrent tumor after surgery, to test the capacity of this treatment to prevent relapse.

Colorectal Cancer

Cancers of the colon and rectum are among the most common malignancies in man. More than 100,000 cases are reported yearly. The primary mode of therapy in the treatment of colon cancer is surgical resection. Only 40% of all patients are curable by surgery alone. New modalities of therapy were needed for those patients who developed recurrent disease or who had metastatic cancer at the time of diagnosis.

Colon cancer was thus targeted for extensive new drug testing in 1971. During the past eight years 40 potential anticancer drugs have been screened for antitumor activity in patients who have advanced colorectal cancer. These studies have identified seven drugs that have some degree of therapeutic effect.

In 1975 the first evidence of the greater therapeutic effect of a drug combination over available single agents was reported. The combination produced a response rate of 43.5% compared to 17% for the single drug, and these data were subsequently confirmed. Drug adjuvant trials, using this combination of drugs with or without immunotherapy in patients at high risk of developing tumor recurrence, are now in progress but are still coded.

Radiation therapy has likewise undergone a great deal of evaluation in rectal cancer during the past

eight years. The Mayo Clinic demonstrated an improvement in survival in patients with locally advanced disease when chemotherapy was added to radiotherapy in the treatment of this disease. This observation is now under further test. NCI funding, $4,570,000, 1972-1978.

Gastric Cancer

For the first time, the effectiveness of several drugs against advanced gastric cancer has been identified in the past five years and even more favorable responses have been noted using these drugs in combination. Although the impact of these studies on survival of patients with metastatic stomach cancer has been modest to date (an increase in median survival from six to 13.5 months), the availability of these drug regimens has offered the opportunity to initiate adjuvant chemotherapy studies in patients with stomach cancer. Early results of these trials also show an improved survival for treated patients. NCI funding, $2,448,000, 1974-1978.

Bladder Cancer

Prior to 1972, the five-year survival in patients with bladder cancer treated with radiation or surgery alone was consistently less than 30%. Now more than half the patients subjected to these treatments in combination survive five years. Those patients demonstrated to have tumor sterilization from radiotherapy have a consistently superior survival. Radiation sensitizers offer hope of increasing this effect further. Two drugs, adriamycin and cis-platinum, have recently been identified as having antitumor effect against advanced bladder cancer and are now under test in drug adjuvant trials. NCI funding, $726,000, 1974-1978.

Malignant Melanoma

This skin tumor is among the most lethal of human cancers. Its incidence is increasing, presumably because of the increased exposure of the population to sunlight. Strides have been made in the surgical diagnosis and staging of this disease, defining groups of patients at high risk of developing recurrent tumor after surgery alone and, thus, paving the way for drug and immunotherapy adjuvant studies. In 1977, a controlled clinical trial indicated that extensive lymph node dissection, previously a routine medical practice, was unnecessary. Another recent adjuvant study has documented an advantage to patients given chemotherapy with DTIC, with or without immunotherapy using the immunostimulant BCG after surgery.

NCI has supported efforts in early diagnosis and staging and the major clinical trials by grants. The World Health Organization trials demonstrating the usefulness of DTIC and BCG have relied on NCI funds for data collection. NCI funding, $2,109,000, 1974-1978.

Brain Tumors

There has been a moderate but definite improvement in survival of adult patients with malignant brain tumors treated with radiotherapy and chemotherapy after surgery. Such trials followed the observation, made prior to 1971, that nitrosourea derivatives induce tumor regression. Current studies are exploring the use of the newly developed radiosensitizer drugs to improve the effects of radiation.

Financial support for the Brain Tumor Study Group research in both the combined modality approach and initiation of clinical trials with radiosensitizers, was supplied totally by NCI. Funding, $5,173,000, 1972-1978.

Head and Neck Cancer

Since 1971, better control of local tumor in the head and neck region has been achieved using radiotherapy coupled with reconstructive surgical techniques developed in the 1960s. With better local control, recurrent cancer outside the treatment field in patients who are living longer has emerged as the major therapeutic hurdle.

New drug testing against this tumor was thus accelerated in the past five years and the positive antitumor effect of bleomycin, cis-platinum and high-dose methotrexate has been identified and confirmed. NCI is now supporting a Head & Neck Cancer Study Group to study the impact of chemotherapy added to surgery and radiotherapy before metastases appear. The Radiotherapy Oncology Group has been fully supported by NCI for the head and neck clinical trials. NCI funding, $3,602,000, 1972-1978.

The balance of the NCI statement, describing major new drugs and advances in other modalities, will appear in subsequent issues of ***The Cancer Letter*** *along with statements by other Cancer Program advocates.*

NCI CONTRACT AWARDS

Title: Programming services in support of the NCI contract management system
Contractor: Sigma Data Services Corp., $123,840.

Title: Development of H-2 recombinant and mutant strains
Contractor: Washington Univ., $83.455.

Title: Cell mediated immunity to rodent tumors
Contractor: Litton Bionetics, $208,116.

Title: Xenotransplantation resource for studies of carcinogenesis in human tissues, supplemental agreement
Contractor: Litton Bionetics, $603,693.

Title: Transplantation, induction and preservation of plasma cell tumors in mice and the maintenance of special strains
Contractor: Litton Bionetics, $1,243,555.

Title: Breast Cancer Detection Demonstration Project, renewal
Contractor: St. Vincent's Medical Center, Jacksonville, Fla., $255,985.

that is not perfection, that spells paralysis."

The most ardent advocate of thymidine is John Stehlin, of the Stehlin Foundation for Cancer Research in Houston. Stehlin and his staff defended their studies, reporting that animal tests had demonstrated effectiveness. Stehlin's laboratory director, Beppino Giovanella, tested the drug on himself, taking 180 grams IV over 24 hours, and said there had been no effect.

Stephen Howell, Univ. of California (San Diego), conducted preclinical tests on mice under a contract from DCT, and told the committee that he had observed no significant tumor response.

Stehlin's pathologist presented slides taken at autopsy of patients who had been treated with thymidine. He pointed out various apparently damaged tumor cells, contending those could have been the result of thymidine treatment.

The pathologist's slides identified several of the patients by name (highly unusual in public presentations by clinical investigators). Schein asked if one of the patients named had had prior therapy (which could have caused the tumor cell damage). Stehlin said he had had no therapy for three months prior to coming to Texas.

"Well, Dr. Stehlin," Schein said, "Mr. _____ was a patient of mine (at Georgetown Univ. Hospital) and had just completed four courses of 5-FU before he got on the plane to Texas. You obviously do not have good histories of your patients. This challenges the credibility of your presentation."

Schein argued that the degree of toxicity work prior to clinical trials was "relatively little. It is an interesting and perhaps important precedent . . . . It is hard to predict a role for thymidine. It may be an expensive method for cell synchronization in anti-leukemia therapy."

DeVita responded that it is "no more expensive than other drugs, and in fact now is cheaper than chlorozotocin."

"Really?" Schein said to accompanying laughter at the needle from DeVita. Schein is conducting a major clinical trial with chlorozotocin and has been closely involved with its development.

Bono said NCI would continue with its plans for phase 2 tests of thymidine.

NCI CONTRACT AWARDS

Title: NCI histocompatibility testing center, continuation
Contractor: Duke Univ., $257,453.

Title: Ten additional alteration/renovation/maintenance/upgrading projects at Frederick Cancer Research Center, modification
Contractor: Litton Bionetics, $339,432.

Title: Microcirculation/molecular transport in mammary cancer, continuation
Contractor: Univ. of Arizona, $84,800.

Title: Breast Cancer Detection Demonstration Project, extension
Contractor: Samuel Merritt Hospital, Oakland, Calif., $226,366

Title: Operation of a refrigerated repository for biological materials in support of NCI intramural research
Contractor: Microbiological Associates, $314,850.

Title: Comprehensive field and laboratory research program on the etiology and epidemiology of human cancer, continuation
Contractor: Univ. of Southern California, $206,000.

Title: Studies of the molecular biology of oncornaviral proteins, continuation
Contractor: Johns Hopkins Univ., $42,280.

Title: Suppression of endocrine function by systemic agents as treatment of human breast cancer, continuation
Contractor: Pennsylvania State Univ. (Hershey), $180,000.

Title: Assembly and distribution of committee books
Contractor: Expand Associates, Silver Spring, Md., $147,187.

Title: Role of stroma in the growth of neoplastic and preneoplastic lesions of the mammary gland, continuation
Contractor: Stanford Univ., $92,000.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the contract officer or specialist named, NCI Research Contracts Branch, the appropriate section, as follows:
Biology & Diagnosis Section and Viral Oncology & Field Studies Section—Landow Building, Bethesda, Md. 20014; Control & Rehabilitation Section, Carcinogenesis Section, Treatment Section, Office of the Director Section—Blair Building, Silver Spring, Md. 20910.
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP N01-CO-95465-09

Title: *Acquisition, indexing and keyboarding of cancer-related meeting and dissertation abstracts*
Deadline: *Approximately Aug. 5*

The International Cancer Research Data Bank Program located in the Office of International Affairs of NCI is requesting proposals for acquisition, indexing and keyboarding meeting abstracts and dissertation abstracts of cancer-related documents.

The output of these operations will be magnetic tapes containing complete bibliographic citations,

abstracts, and index terms assigned to the selected documents. On delivery of the tapes to the ICRDB, the data on the tapes shall become the property of NCI to be used as needed in any type of automated system or technical document without any restriction or payments other than those required for preparation and delivery of the tapes as covered by this RFP.

Lists of pertinent meetings will be delivered to the contractor each month. The contractor shall then obtain and screen the proceedings of professional meetings for cancer-related abstracts of papers presented at those meetings. The contractor shall then obtain and screen the proceedings of professional meetings for cancer-related abstracts of papers presented at those meetings. The contractor shall also obtain and screen dissertation abstracts for cancer-related abstracts. It is anticipated that a maximum of 12,000 abstracts dealing with cancer-related topics will be identified each year. These abstracts shall be revised, indexed, coded and keyed in a format and style designated by the project officer and shall be converted to magentic tapes as outlined in the sections below.

The organization selected must undertake the tasks outlined above and prepare the magnetic tapes in the shortest possible time, using highly qualified biomedically trained personnel experienced in screening, abstracting, and indexing of biomedical literature and computer personnel skilled in the preparation of magnetic tapes containing citations, abstracts, and index terms.

Personnel engaged in indexing must have been trained by the National Library of Medicine in the MeSH (Medical Subject Headings) indexing techniques.

Special attention is directed to the "small business representation" of this solicitation and the "small business size standards" of this solicitation. Failure to meet the standards as specified shall render a proposal nonresponsive and ineligible for award of a contract. This effort is considered a data processing category and firms must have average annual receipts, for the preceeding three fiscal years, of less than $4 million. The proposed procurement listed herein is 100% set aside for small business concerns.

RFP N01-CO-95463-09

Title: *Screening, abstracting and indexing of cancer-related literature*

Deadline: *Approximately Aug. 5*

The International Cancer Research Data Bank Program is requesting proposals for a contract to screen a minimum of 1,500 biomedical and scientific journals as well as other documents (such as books, proceedings of meetings, technical reports, etc.) in order to identify approximately 40,000 articles related to cancer each year.

All of these articles shall be indexed using the National Library of Medicine Medical Subject Headings vocabulary. Approximately 15,000 articles shall be selected for abstracting and keyboarding each year. In addition, approximately 25,000 author abstracts, and other prepared abstracts, shall be selected for keyboarding only.

A magnetic tape containing complete bibliographic citations, abstracts, and index terms shall be prepared and delivered on a weekly basis. The maximum time permitted between receipt of an input source document and delivery of the magnetic tape shall be four weeks.

The organization selected must be prepared to provide the above in the shortest possible time using highly qualified, biomedically trained personnel experienced in screening biomedical literature and writing biomedical abstracts; and experienced data processing and managerial personnel.

Contract Specialist for the above 2 RFPs: Gloria Dahl
Office of Director
301-427-7984

RFP PL-79-34-JLW

Title: *Clearinghouse for smoking and health information*

Deadline: *Not available*

The office of smoking and health contemplates a contract for information support to continue its clearinghouse role and responsibilities for the collection and dissemination of smoking and health information. The proposed contract will include scanning and processing of scientific and technical literature, compilation of registries of ongoing research, computer and microfilm processing of bibliographic data, provision of camera-ready copy for specific publications on smoking, user awareness and evaluation of services, inquiry response, and other information support tasks as specified.

Prospective offerors will be required to submit offers reflecting planned subcontracting opportunities to small and disadvantaged business concerns. The proposed offers shall provide for, as a minimum, 15% of proposed cost to be subcontracted to such concerns.

Contracts Branch
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