THE CANCER LETTER

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FDA SUBCOMMITTEE LEANING TOWARD MOUSE-DOG DRUG TESTING FOR NEW PRECLINICAL TOXICITY PROTOCOL

The subcommittee of the FDA Oncologic Drugs Advisory Committee set up to study NCI's proposals for new preclinical toxicology protocols is leaning toward "Option B" (*The Cancer Letter*, June 15), which would permit use of mice and dogs and ratify the abandonment

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In Brief

OBEY WAS RIGHT — TESTS ON 70 CHEMICALS WOULD HAVE BEEN ABORTED UNDER NCI BUDGET

DAVID OBEY was correct in stating that if NCI's Carcinogenesis Testing Program receives no more than the same amount of money in FY 1980 that it is getting in 1979 ($22 million), 70 of the 195 compounds currently on test would have to be dropped before the tests are completed (*The Cancer Letter*, July 13). Before Obey and the House HEW Appropriations Subcommittee ordered $23 million reprogrammed into the testing program, however, NCI had already shifted additional funds to reduce the number that would have to come off test to 42 and was looking for other money in an effort to keep all 195 tests going. The additional $23 million would do that plus permit initiation of tests on a substantial number of additional chemicals. . . . **JOHN BENNETT**, professor of oncology in medicine at the Univ. of Rochester Cancer Center, is the new chairman of the Clinical Cancer Investigation Review Committee, which reviews Cooperative Group grants. He replaces Jerome DeCosse, whose term on the committee expired July 1. . . . **UNIV. OF KANSAS'** Mid America Cancer Center, in Kansas City, may be the next to seek recognition as a comprehensive cancer center. C.C. Cheng is director, Barth Hoogstraten heads clinical research. . . . **GOVERNMENT SURVEY** of federal employees eligible for the Senior Executive Service found that 87% regard themselves as among the top 10%. Pay increases and bonuses offered by SES will depend on performance evaluation; that top 10% is going to be very crowded. . . . **FIBROUS GLASS** dust reported as possibly the cause of pneumoconiosis in a Japanese woman with occupational exposure to glass wool insulation was exonerated in a further study of the case. NCI Director Arthur Upton said in a special communication that the new study of the case, first reported by Tatsuo Sano last November, turned up the information that the woman had a previous exposure to asbestos, and that asbestos fibers were found in the transbronchial biopsy. . . . **COUNCIL FOR TOBACCO** Research noted on its 25th anniversary that it has awarded $51.9 million to 379 investigators in 247 institutions since 1954 for research on smoking and health.

SUBCOMMITTEE FAVORS OPTION B PROPOSAL FOR NEW PRECLINICAL TOXICITY TESTING

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of the monkey in animal toxicity testing.

Div. of Cancer Treatment Director Vincent DeVita and Experimental Therapeutics Program Director Vincent Oliverio and their staffs preferred "Option A," which would require only tests in mice. The difference in costs: $56,000-60,000 per compound for Option B, $12,000-15,000 for Option A (compared with $100,000-120,000 with the present protocols).

NCI also had asked that histopathology not be required until some therapeutic benefit is seen in phase 2 trials. The present protocol calls for histopathology before phase 1 trials.

Some subcommittee members agreed that Option A would provide sufficient toxicity data, but the majority seemed to favor Option B, with some modification of doses. They felt that there is a lack of qualitative correlation of organ toxicity from mouse to man, a correlation which has been established in dogs.

DCT has a contract with Battelle to determine the mouse-man correlation, and Oliverio said that data would be available within two years.

The subcommittee also did not go along with the NCI proposal on histopathology, although a compromise may be reached, with histopathology required after phase 1 tests instead of before.

NCI had hoped that by reducing the toxicity costs and time required to complete them, universities and other research institutions would be encouraged to undertake their own independent drug development programs. Option A would have done that, while the cost reduction with Option B probably will not.

The subcommittee will make its recommendation to the full Oncologic Drugs Advisory Committee, where the proposal could be further modified. The committee's next meeting is Oct. 11-12.

In any event, the full committee's decision will only be a recommendation. FDA staff, through the commissioner, will make the final determination, probably after publishing the proposed new protocols in the *Federal Register* and soliciting comment on them.

CALGB LOSES GRANT FOR PEDIATRICS COMPONENT; HODGKIN'S MEETING OKAYED

Grant support for the pediatrics division of Cancer & Leukemia Group B was denied for the second time by the Clinical Cancer Investigation Review Committee at the committee's June meeting.

The CCIRC last November disapproved CALGB's renewal application for its pediatric activities. The group responded by reorganizing its pediatric component as a division, cochaired by Barbara Jones of West Virginia Univ. and Gerald Gilchrist of Mayo Clinic. A new grant application was submitted, but following site visit and review, the committee once again disapproved it.

The action does not affect the extensive adult clinical trials conducted by CALGB.

Other items discussed by the committee included:

- The proposed symposium on Hodgkin's disease, scheduled for September 1980, in San Francisco, if CCIRC's grant to support it is funded. The committee was told that the grant had been approved by an NIH Div. of Research Grants study section, but with a modest priority score. The Div. of Cancer Treatment has the option of funding it if it so desires; the grant would be for less than $35,000 and thus would not require concurrence of the National Cancer Advisory Board.
- The Cooperative Group budget for the 1980 fiscal year, which it appears now will be the same—$31.5 million—the Groups are getting in the current fiscal year.
- The proposed new funding mechanism, the cooperative agreement. Edwin Jacobs, associate chief of the Clinical Investigations Branch, said that DCT plans to convert contracts to cooperative agreements first, to gain some experience with the mechanism before switching over any grants to it.

NCAB MEETING POSTPONED TO OCTOBER IN NIH PUSH TO MEET EMPLOYEE CEILING

The National Cancer Advisory Board's September meeting has been postponed to Oct. 3-5 as a result of a congressional mandate on personnel ceilings. Meetings of contract review committees, originally scheduled during the period from Aug. 26 to Sept. 22, have been postponed to later dates, for the same reason.

In the Civil Service Reform Act approved last year by Congress, a provision was included requiring that the total number of federal employees reported on the payroll as of Sept. 30, 1979, could not exceed the total number that was on the payroll as of Sept. 30, 1977.

Part time employees are included in those totals. Members of certain advisory groups, boards and review committees and consultants to those bodies are considered part time employees during the pay periods in which they meet.

NIH has not been able to reduce its number of employees to the required ceiling despite being under an HEW wide restriction since June 23 of hiring only one permanent employee for every three vacancies that occur.

NIH Director Donald Fredrickson, faced with the alternative of furloughing all part time employees, chose instead to try to achieve the necessary reductions by rescheduling committee meetings. Members of those groups thus will not show up on the NIH payroll as part time employees during the final pay period of the fiscal year.

Members of review groups whose stipends and expenses are paid from grants are not considered part time employees. Those, which include all of the NCI grant review committees, are therefor excluded from the September meeting ban, much to the relief of NCI executives.

"It would have been a catastrophe if it had affected site visits," said Thomas King, director of the Div. of Extramural Activities. The result probably would have been that many grants would have missed an entire review cycle.

Dates of NCAB meetings are established more than a year in advance, to permit members the opportunity to adjust their schedules. The late change probably will keep some members from attending, although King still expects to have a quorum.

AACI GROUP DEVELOPING NEW GUIDELINE SUGGESTIONS FOR CANCER CONTROL GRANTS

Suggestions for new guidelines for cancer control core grants to cancer centers are being developed by the Task 12 committee of the Assn. of American Cancer Institutes. Joseph Painter, chairman of the committee, reported at the recent AACI meeting that committee had organized a meeting of all center cancer control directors who agreed:

"We needed a thorough definition of cancer control, what the priorities were, where we were going from a program management standpoint," Painter said. "We needed more time to get programs started. The review process is somewhat different, and it became apparent we needed a better definition of what it was all about."

Painter said the committee has undertaken "a major effort to rewrite cancer control grant guidelines." That effort will address "the need for prolonged support of community programs; define types of core support personnel, to include the director, investigators, and staff for evaluation and community relations; and shared resources from the centers or parent institutions."

Another major issue is the growing importance of evaluation, Painter said.

Jan Steiner, director of the Illinois Cancer Council, objected to what he called the "divisive RFP" issued by the NCI Div. of Cancer Control & Rehabilitation for the Community Hospital Oncology Program. The RFP specified that participating hospitals have no existing formal relationship with cancer centers or universities. "That is obviously divisive," Steiner said. "I hope Bill Terry (DCCR acting director) takes back AACI's opinion that RFPs should take cognizance of the determination of the Assn. of Community Cancer Centers and AACI to work together."

"That is worth considering," Terry said. "I hope in the future there will be fewer RFPs and more grants."

R. Lee Clark, president-emeritus of the Univ. of Texas System Cancer Center, brought up the question of combining cancer control core grants with the regular core support grants. William Shingleton, director of the Duke Univ. Comprehensive Cancer Center and chairman of NCI's Cancer Control & Rehabilitation Advisory Committee, pointed out that had been discussed by the National Cancer Advisory Board.

John Durant, director of the Univ. of Alabama Comprehensive Cancer Center, said, "It is an exhaustive process to review the sceintific core grant alone, requiring as much as three days. To have the control review at the same time would be too much. I would like to suggest that we get the two reviews into the same cycle, but not on the same day."

Steiner and Durant noted that some review of control grant applications has not included site visits. "That has got to stop," Durant said.

John Laszlo, director of clinical programs at the Duke center, reported in a letter presented at the meeting on the status of the Statistical Analysis Quality Control/Cancer Center Patient Data System Program:

"The CCPDS project is going extremely smoothly, particularly when one considers its turbulent beginnings," Laszlo wrote. "Though some of the comprehensive cancer centers were slow to develop their minimal data base programs, all but one of the comprehensive cancer centers are participating as far as I'm aware and the relationship of these centers with the statistical office in Seattle has been truly superb. The statistical office has had its contract renewed and the participating centers have submitted their own grant renewals as of June 1, 1979, for those centers which began the funding process simultaneously (others are in a different cycle). We are very optimistic that there will be continued funding for this program. Towards this end we have had meetings with NCI representatives including Dr. William Terry and I believe that they are fully supportive of the role of this important cooperative effort.

"It's too early yet to comment on the results of the studies to date, but interesting trends regarding differences in histologic diagnoses of certain tumors and in methods of treatment are already becoming apparent. There are going to be many important leads that bear on differences in tumor classification and treatment which will need to be followed up.

"I would like to inform the AACI members that we have been working much more closely now with the American College of Surgeons and its new leader, Dr. Charles Smart. Dr. Feigl and I addressed the college at a meeting in February 1979 to both discuss the SAQC/CCPDS Program and to offer suggestions as to how the American College of Surgeons might better relate with comprehensive cancer centers. We have put rather forcefully the willingness of the centers to work together with the college in its efforts to upgrade tumor registries and at the same time have emphasized that some of the past accreditation policies of the college have impeded orderly

progress. We would like to see much of the developmental work towards validating staging systems be done in the comprehensive cancer centers and data provided to the college and to the American Joint Committee. We have good liaison in these regards with Dr. William Taylor of the Mayo Clinic. Dr. Smart has reciprocated with his interest in our program and will be addressing the CCPDS group.

"An early hope of Dr. Robert Hickey and others was to extend the minimal data base towards research goals. There is an active research committee working on a number of different projects of mutual interest to the centers. We will report on this further at the next AACI meeting," Laszlo concluded.

Alvin Mauer, medical director of St. Jude Children's Research Hospital, reported on the Task 10 committee's consideration of the issues of reimbursement for administration of anticancer agents which have not been approved for marketing by the Food & Drug Administration, and patient injury compensation.

NCI has grouped those drugs into three categories—Group A, essentially those in phase 1 testing; Group B, primarily phase 2; and Group C, those for which some antitumor efficacy has been demonstrated but which have not yet been approved by FDA for marketing. Some drugs which have been approved for certain indications are considered group C for other indications. NCI makes group C drugs available to practicing physicians at no charge, and will supply group B drugs to physicians working with cooperating cancer centers or other recognized groups.

Earlier this year, it was reported that some institutions had been unable to obtain reimbursement from Medicare for administration of group C drugs. There was concern that if the practice of not reimbursing for treating patients with experimental drugs became widespread, clinical cancer research could be severely hampered.

Mauer's report:

"At the meeting in January 1979, some members indicated that they were having difficulty recovering reimbursement from insurance companies for the administration of chemotherapeutic agents in the categroy C group. It was obvious that this was not a widespread problem but there was concern that if it existed in some localities, it might spread to become a more general practice. The Association asked the Task 10 committee to look into this matter and to see what could be done to alleviate the situation.

"An attempt was made to find out how widespread the practice of withholding reimbursement for the administration of category C drugs was. It turned out that, at this time, the practice was quite limited and that only a few member organizations had experienced any difficulty. At this time also, the Div. of Cancer Treatment of NCI began discussions with the administrators of Medicare and Medicaid concerning the matter of reimbursement for these treatments. It was felt that if a policy were set at this level it would be followed by insurance carriers. DCT has been asked to prepare a paper on the topic for submission. DCT is in that process and will request that drugs in category C and also categories A and B be eligible for reimbursement. The white paper will make the point that these patients are being treated according to accepted protocols and that at the time these drugs are being given the therapy represents the most reasonable and effective regimen for the cancer patient at that stage of the disease. While several months may be needed for completion of this action, it is anticipated that this white paper will be accepted and its recommendations approved.

"Late in 1978, HEW released an interim final regulation concerning compensation for injury acquired during the course of research involving human subjects. The regulation became effective as of Jan. 2, 1979, and was released without an appropriate period for comment. Subsequently, it has been determined that this release is questionably legal and certainly its manner of release not according to established administrative procedures. It has received wide comment and criticism. It became apparent that additional regulations were being considered which would have mandated the provision of compensation for injury.

"Information has been obtained concerning the status of development of regulations which would mandate compensation. It soon became evident that it would be advisable to have a conference for which the committee could act as a resource involving the group responsible for the NCI/DCT study of the effects of regulations on the conduct of cancer research. In conjunction with Richard Olson of the Univ. of Pittsburgh, the plans for this meeting are under way and it should be held some time within the next couple of months. It is hoped that out of this conference will come a report concerning the matter of compensation for injured research subjects and its implications for clinical research in cancer, especially clinical therapeutic research."

MORE EXCERPTS FROM PRESENTATIONS AT COMMITTEE ON AGING HEARINGS

The leading cancer scientists who appeared before Claude Pepper's Select Committee on Aging last month presented summaries on a variety of aspects of the National Cancer Program, much of which had not yet been seen in print. ***The Cancer Letter*** published excerpts from some of those presentations in the June 29 issue. Selections from others follow:

Gerald Murphy, director of Roswell Park Memorial Institute—Your committee must be aware by now that while almost 50% of all cancer patients can now be saved, there are unfortunately significant numbers of cancer patients in our nation who are not getting the best that is potentially available to them. To remedy this situation, we are training cancer workers at most of the nation's 70 cancer centers. In the

period from 1975 to 1979 we have gone from the training of 200 nurse oncologists a year to 1,700. In the training of medical oncologists, we project an increase from 1,130 this year to 1,846 in 1980, and 3,165 in 1985. Similarly it is anticipated that the number of surgical oncologists will increase by 63% in 1985. Many of these individuals are being trained in the schools and hospitals associated with our cancer centers, insuring that these men and women will emerge with the latest available knowledge rather than academic information alone that would need to be followed by on-the-job training. To produce these numbers of trained clinical practitioners, it is clear that those funds presently available for training in cancer will have to be substantially increased if the needs of our citizens are to be met.

David Paulson, VA hospital, Durham, N.C.—Unfortunately, once [prostatic cancer] has been diagnosed and the extent of disease determined, there currently exists little hard data on which to base treatment decisions. The two major treatment alternatives are surgery, which produces 5, 10 and 15 year survival rates of 72%, 50% and 29% respectively, and radiotherapy, which produces 5 and 10 year survival rates of 70% and 60% respectively. These survivorship figures are based on data derived prior to the recognition of the inaccuracy of earlier methods of clinical staging.

The problem in treatment evaluation is simply this: There are no ongoing studies which randomly assign patients with early stage disease to one or another treatment program in order to evaluate the relative disease control of each treatment. The overall lack of controlled clinical trials in prostatic cancer in general was recently witnessed by the failure to describe progress in treatment of prostatic cancer in the Clinical Trials Review held 26-27 March 1979.

The single study which had promise of evaluating the disease control impact of surgery versus radiotherapy for localized disease and radiotherapy versus delayed hormonal therapy for regional disease apparently will not be afforded continued support despite the fact that over 325 patients have already received randomized treatment, despite the fact that the preliminary findings imply that there is a difference in disease control between surgery versus radiotherapy for localized treatment, and radiotherapy versus delayed endocrine therapy for regional disease. Let me stress that 325 patients represents one-half of the total number necessary to complete this study. Failure to pursue this study to completion will perpetuate the current practice of making treatment decisions as to surgery, radiotherapy or delayed endocrine therapy, based on physician bias rather than fact.

Gerald Rosen, Sloan Kettering—The current projected five year survival rates for children with malignant bone tumors at our cancer center are in excess of 80%. The most common of these bone tumors, osteogenic sarcoma, was once considered the most resistant tumor to treatment, and following surgical treatment alone, less than 20% of patients would be expected to survive for more than five years. It is in this latter group of patients that I have spent most of my time doing clinical investigations to achieve a disease free survival rate of more than 80%. Although there may be only approximately 1,000 patients per year in the United States with malignant bone tumors in the pediatric and adolescent age group, the success in the treatment of these patients can serve as a model for attacking some of the more resistant and common tumors of the adult population.

These latter tumors include some of the major problems in the aging, including lung cancer, colon cancer, advanced breast cancer, and pancreatic cancer. I hope this model of treatment will point to the fact that the best hope for the future is not some new miracle drug, but the optimal use of existing modalities of treatment and the restructuring of our health care delivery system, making it possible to give the aggressive treatment needed to obtain cures, in the large segment of our older population that needs this type of treatment. . . .

Because of our success in the treatment of musculoskeletal sarcomas in the pediatric and adolescent age group, I had been asked to treat adult patients in the Dept. of Medicine with soft tissue and bone sarcomas. Osteogenic sarcoma is also a disease of older people since it occurs as a secondary complication of Paget's disease. Osteogenic sarcoma arising in Paget's disease in the older patient is a very rapidly lethal disease, even when radical surgery can be done. In the past few years I have embarked on trying to treat some of these older patients. However, the lack of an ambulatory day hospital for adults made it mandatory for me to try to admit patients to the hospital for each treatment. It had been said that we were more successful with pediatric tumors because children tolerate more drug than adults do. This is not true. The adults can tolerate just as much drug as do the children, however, we have to be very agressive with the treatment, and have the facilities not only to give the treatment, but to support the patient through the resulting toxicity that may occur. The lack of an ambulatory care day hospital in which to treat even a few adults has made it very difficult not only to give the treatments, but to find a bed to admit the patient and to give the drug on schedule.

It has become apparent that the large numbers of adult patients with cancer cannot be accommodated by our current health care delivery system if we are to use intensive drug therapy. There are not enough hospital beds in which to treat these patients. Furthermore, pediatric patients would receive a three day treatment in our day hospital and the cost would be only three days at half the inpatient rate. I found that every time an adult was admitted, it would take approximately five days of hospitalization at the full

inpatient reimbursement rate to give that patient three days of treatment. That meant that it was approximately 333% more expensive to give the same treatment to an adult as to a child who had an ambulatory setting in which to receive the treatment. In addition, the ambulatory setting made that treatment more efficient, more successful and safer because it could be carried out on schedule and continuing supportive care could be given after the treatment.

Philip Schein, Georgetown Univ.—In 1974 the Div. of Medical Oncology of the Lombardi Cancer Research Center of Georgetown Univ. developed a three drug combination which incorporated the most active anticancer agents for gastric cancer: 5-fluorouracil, adriamycin and mitomycin-C. This regimen, now known as FAM, was designed to be used as outpatient treatment and with low toxicity so as to insure that the patient's quality of life would be preserved. We have recently reviewed our results in the treatment of 61 cases with advanced stages of gastric cancer. The average age of this patient population was 62 years, the oldest being 83 years of age. Approximately 45% of our cases evidence at least a 50% reduction in the size of the tumor mass, with an average response duration of 10 months. The median survival of these responding patients is 14 months with several patients alive from 2 to 3 years with good quality of life. It must be re-emphasized that all of these patients had large masses of tumor involving vital organs such as the liver, a patient population with an otherwise extremely poor prognosis. Collectively, these data are quite similar to what is currently being accomplished with combination chemotherapy of advanced breast cancer, a recognized drug-sensitive tumor.

The activity of our FAM has now been confirmed in a controlled trial conducted by the Southwest Oncology Group. A similar regimen has recently been compared with the standard 5-fluorouracil-nitrosourea combination, and FAM produced a two-fold increase in patient survival.

These results demonstrate that gastric cancer, even in its most advanced stages of spread, is a potentially treatable tumor. We have also shown that the advanced age of our patients did not preclude effective and well-tolerated treatment.

The major emphasis of recently initiated clinical trials is being directed to patients with less advanced disease. The initial results, from a completed study conducted by the Gastrointestinal Tumor Study Group, look quite promising. In this program, combination chemotherapy was compared to radiation therapy followed by chemotherapy. The patient population, which had an average age of 60 years, all had tumor that could not be completely resected, but which was still confined to the region of the central upper abdomen. Cancer chemotherapy used alone produced a significantly superior survival and less adverse reactions. Some 40% of patients are alive at two years of followup, and importantly the patients whose age was greater than 60 years have lived significantly longer than the younger age group. This result was achieved with a form of chemotherapy that we now recognize as having inferior activity when compared to the FAM regimen. This demonstrates that chemotherapy will produce its best results in patients with a limited tumor burden. In the past this requirement was seldom fulfilled, and patients were treated with drugs only after all other measures had failed and the extent of tumor was well beyond the capacity of the type of chemotherapy employed.

Emil Frei, Sidney Farber—A significant reduction in [nausea and vomiting] can be achieved with the class of drugs known as the phenothiazines. Recent chemical modification of this class of drug has led to derivatives (the piperazine class of phenothiazines) which are much more effective experimentally and in preliminary studies, clinically with respect to reducing nausea and vomiting.

In 1974 Sallan et al demonstrated that THC, a derivative of marijuana, significantly reduced nausea and vomiting in patients receiving chemotherapy. A chemical modification of THC known as nabilone is highly effective both experimentally and clinically in this setting. More recently, fat soluble opiate drugs such as fentanyl have been prepared which show great promise in controlling nausea and vomiting.

Finally, hyperalimentation significantly reduces nausea and vomiting in patients receiving chemotherapy. In summary, this difficult side effect of chemotherapy is coming increasingly under control with an associated marked improvement in the quality of life.

Another side effect of chemotherapy is loss of hair. . . . A recent study by Dean employing a technique that delivers pressure and cooling to the scalp for 30 minutes prevents the chemotherapeutic agent from damaging the hair follicle and reduces hair loss almost totally in 50% of such patients and substantially in an additional 30%. The technique is simple, acceptable to patients, and bids well to control this important and difficult side effect.

Joseph Bertino, Yale—The cornerstones of treatment of head and neck cancer are radiation therapy and surgery. Surgery is used when there is a reasonable anticipation that treatment will afford the opportunity for cure and that it will be more effective than radiation therapy or if equally effective it will shorten the time for treatment. Radiation therapy is most commonly applied in the form of an external beam, but interstitial treatment is also utilized. The major advance in head and neck radiation therapy was the development of high energy sources such as cobalt, betatrons and linear accelerators. Supervoltage therapy has permitted the delivery of fairly uniform high-doses of radiation to deeply seated

lesions without excessive radiation of surrounding normal structures and with relative sparing of the skin and bone. . . .

Despite advances in surgical and radiation techniques, overall dismal figures emphasize that optimum treatment has yet to be achieved for head and neck cancer not only for advanced disease at all sites but even early disease at certain sites as the gingiva, tonsillar fossa, pyriform sinus and nasopharynx. Therefore studies are in progress on the effects of chemotherapy used together with surgery and/or radiation therapy in an attempt to improve curability. Several early reports of encouraging results using various combined modality programs that include chemotherapy have been reported. . . . The highest priority for future trials will involve studies that involve multiple modalities which include chemotherapy plus radiation and surgery.

Robert Young, NCI—The unique behavior of ovarian cancer as it spreads may actually provide us with a unique opportunity to use drugs more effectively in its treatment. Ovarian cancer almost always remains confined to the abdominal space even when the tumor becomes advanced. A series of studies are now underway at the Medicine Branch, DCT, NCI, using the direct intra-abdominal administration of drugs. With this technique, very high concentrations of drug can be produced in the abdominal cavity which directly expose the tumor to concentrations of drug far in excess of that which can be achieved by conventional drug administration. The unique pharmacologic effect of intra-abdominal chemotherapy is that it not only exposes the tumor to high concentrations of drug but it produces a substantial reduction in the toxicity of the drug to other more distant organs. The use of unique methods of administration of chemotherapeutic agents may improve therapy of ovarian cancer.

It seems clear from all the recent studies reported in the past five years that major efforts to systematically investigate a wide variety of important treatment options have been undertaken by oncologists from diverse clinical backgrounds. A burst of interest and enthusiasm has replaced the fatalistic view so prevalent even 10 years ago. This spark of interest and sustained research effort cannot help but benefit women afflicted with this illness. The death of one woman in the United States every 50 minutes should be a sufficient driving force to stimulate us to redouble our efforts at new and innovative approaches to the treatment of ovarian cancer.

Willet Whitmore, Sloan Kettering—Bladder cancer represents a spectrum of diseases with a tendency to multicentricity over time that warrants its consideration as a chronic disease. Studies of the etiology and epidemiology will provide important leads regarding causation and risk factors which will be helpful in designing methods of prophylaxis and in defining high risk groups for which screening techniques may be applicable. Diagnostic methods are highly efficient when applied to the bladder tumor suspect. Assessments of the host, of the existing tumor, and of the risk of new tumor formation in the diseased bladder are important to optimal therapy. Endoscopic treatment of superficial tumors is highly effective in the control of the existing lesions but offers no prophylaxis against new ones. Better definition of "predictors" will permit identification of those patients who are at highest risk of new tumor formation and may ultimately better define a population of patients in whom prophylactic cystectomy is justified. In patients with deeply infiltrating tumors combinations of irradiation and surgery have improved end results but have simultaneously defined distant dissemination as a common cause of treatment failure. The development of effective systemic adjuvant therapy (chemotherapy and/or immunotherapy) will further prospects for cure in such high risk patients. For patients presenting with distant dissemination systemic chemotherapy offers the greatest hope for benefit.

H. Marvin Pollard, past president of the American Cancer Society—Pioneering done by the Society in the mid-40's is being matched today with a tremendously exciting new bit of research administration which we call our Research Development Program, started a year ago.

This new program is able to achieve the startling result of receiving, reviewing, evaluating and awarding a research grant on a routine basis within 90 days and often faster. This new program is the private sector's answer to the highly inspired, motivated, enthusiastic scientist who is simply not equipped to deal with more cumbersome administrative procedures. It is a one-shot award aimed to keep him inspired and moving while longer term support is being arranged by himself or others. The award has an upper dollar limit of $50,000, and an upper time limit of 18 months. So far $4.2 million Society funds have been invested in 55 grants under our Research Development Program. Awards are made on the basis of ideas having unusual merit, or special urgency, which promises success in clinical treatment or in prevention of cancer. If an ongoing research project hits a snag because of an unexpected need for equipment then our new system swings into action.

(Pollard noted that awards under that program included support for research with vitamins C, E and A; interferon; hyperthermia; and Kurt Isselbacher's work with galatosyl-transferase in diagnosis of cancer.

(Pollard also mentioned the new ACS Community Coordination Program, which awards "Cause and Prevention" grants to cancer centers, up to $200,000 a year for five years. ACS plans to make 10 such awards initially, and recently approved the first to Mt. Sinai in New York, with Irving Selikoff as the principal investigator.)

SOURCES SOUGHT – 79-V

Title: *Identification of populations for a study of long term maintenance of nonsmoking behavior*

Deadline: *Aug. 22 (for statement of qualifications*

The Div. of Lung Diseases of the National Heart, Lung & Blood Institute is issuing this sources sought announcement to identify groups with the experience and capability necessary to conduct a program with the following long range objective:

Identify modifiable variables associated with success in maintaining long term nonsmoking behavior in former smokers who are known to have early symptoms of chronic obstructive lung disease, or have been exposed to respiratory disease risk factors in addition to smoking.

Research on smoking behavior has concentrated largely on variables predictive of success in smoking cessation. Maintenance of nonsmoking behavior, which has been more difficult to achieve, may be influenced by different variables. For example, little is known about the effect of social environmental processes, such as family or peer support, on maintenance of nonsmoking.

Sources responding to this announcement should have experience in conducting smoking cessation programs and have access to, or the capability of gathering, information about the health status (especially respiratory health), socioeconomic status, age, and sex of individuals who have completed a smoking cessation program and maintained nonsmoking behavior at least six months.

Sources meeting these requirements are invited to submit a letter addressing the following items:

1. Techniques used to achieve smoking cessation.
2. Data on general success of these techniques in influencing smoking behavior a) immediately after completion of the program, and b) after six months.
3. Methods of validating reported smoking behavior.
4. Description of the population group available for study, including characteristics such as age, sex, socioeconomic status, and health status.

The total response, including curriculum vitae, should not exceed 10 pages.

This announcement is not a request for proposal and in no way commits NHLBI to award a contract to any part either now or in the future. To RFP is available. On the basis of the replies to this announcement, the Div. of Lung Diseases will determine whether sufficient interest and capability exist to initiate this program. If an RFP is issued, all qualified organizations or institutions may submit a proposal.

Ten copies of the response should be sent to:

Sydney Ruth Parker
Prevention, Education & Manpower Branch
Div. of Lung Diseases
National Heart, Lung & Blood Institute
6A05 Westwood Bldg
Bethesda, Md. 20205
Phone 301-496-7668

NCI CONTRACT AWARDS

Title: NCI immunodiagnostic reference center, continuation
Contractor: Meloy Laboratories, $319,738.

Title: Central statistical group for collaborative studies in lung cancer, pancreatic cancer, and EMI scanner evaluation (brain cancer), continuation
Contractor: Univ. of Cincinnati, $199,878.

Title: Study on pulmonary tumors in mice for carcinogenesis and cocarcinogenic bioassay
Contractor: Univ. of California (San Diego), $65,103.

Title: Development of new reagents for characterization of subpopulations of human cells imported to the immune response
Contractor: Univ. of New Mexico, $88,398.

Title: Development of 5'-nucleotide phosphodiesterase serum isozyme test for human cancer patients, continuation
Contractor: Univ. of Pennsylvania, $80,613.

Title: Development of topical chemotherapeutic agents for mycosis fungoides, continuation
Contractor: Johns Hopkins Univ., $66,791.

Title: Growth of normal and tumor virus cells, continuation
Contractor: Meloy Laboratories, $218,853.

Title: Use of screening techniques for blood in the stool as a means of detecting early cancer of the bowel, continuation
Contractor: Univ. of Minnesota, $1,375,440.

Title: Operation of a register of tumors in lower animals, continuation
Contractor: Smithsonian Institution, $165,617.

Title: Screening, indexing & abstracting of cancer-related literature for input to the ICRDB program data bases
Contractors: Franklin Institute, Philadelphia, 11-month renewal, $946,414; and MeSH Indexing, 12 month modification, $291,823.

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