THE CANCER LETTER

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1411 ALDENHAM LANE RESTON, VIRGINIA TELEPHONE 703-471-9695

ENVIRONMENTAL EMPHASIS URGED, INCLUDING NEW ROLE FOR COMP CENTERS; NCAB UNENTHUSIASTIC

The National Cancer Advisory Board's Subcommittee on Environmental Carcinogenesis submitted significant and, in some cases, extremely controversial recommendations to the Board this week, but they failed to generate much enthusiasm or even any negative response.

The subcommittee, chaired by Philippe Shubik, made the point when

(Continued to page 2)

In Brief

FIRST CREG ANNOUNCEMENT DUE IN LATE APRIL FOR IN VITRO CARCINOGEN TEST IMPROVEMENTS

FIRST ANNOUNCEMENT of a Cancer Research Emphasis Grant program will be out late in April. NCI will ask investigators to develop proposals for developing new or improved methods of in vitro chemical carcinogen testing. First awards are probably a full year away, however. "I was surprised by the length of time we were asked to allow for development of proposals," said Umberto Saffiotti, associate director for carcinogenesis in NCI's Div. of Cause & Prevention. After guidelines are announced, investigators will have six months to submit proposals. Study section review probably will go on through January, with final review by the National Cancer Advisory Board not possible until the Board's meeting next March. From program inception to award, CREG's elapsed time will be the longest of any NCI funding mechanism. CREG was drawn up by NCI to channel some projects away from contracts into grant programs. . . . **ERWIN VOLLMER** has retired as chief of the breast cancer program coordinating branch in the Div. of Biology & Diagnosis. He joined NCI in 1956, was executive secretary of the breast cancer task force since it was established in 1966. D. Jane Taylor is acting chief of the branch. . . . **RONALD HERBERMAN**, who has headed the cellular & tumor immunology section, has been appointed acting chief of the new laboratory of immunodiagnosis in the B & D division. . . . **NORTON NELSON**, director of NYU's Institute of Environmental Medicine, is one who does not agree with the NCI executive who says prime contractors can run some programs better than the government (*The Cancer Letter*, March 14). Nelson told the NCAB Subcommittee on Environmental Carcinogenesis that delegating responsibility to a prime contractor was an "abdication" of that responsibility by NCI. Further, he refuses to participate in a program controlled by a prime contractor because it is "demeaning" not being able to work directly with NCI staff. . . . **BENNO SCHMIDT** will be reappointed to the President's Cancer Panel and continue as chairman. He met with the President this week. . . . **CONSTRUCTION** funds for Einstein's cancer center will be released by OMB, backing down a little in its refusal to fund new construction. OMB still insists it won't release money for other new construction, contrary to Congress' orders.

Shubik placed the task of encouraging comprehensive centers to establish strong prevention programs at the top of the subcommittee's list of recommendations. "We must point out to the board that we're giving all this money to comprehensive centers which pay no attention to prevention. They maintain records in such a thoughtless manner that they can't be used by epidemiologists. . . . The potential to get something out of them is so great because they are doing so little."

Former NCAB member Arnold Brown, a consultant to the subcommittee, suggested that the recommendation should include explicit statements on what comprehensive centers would be expected to do use of standard patient history forms, training on risk factors, epidemiology, basic studies on carcinogenesis mechanisms.

It was Brown who said NCI should force centers to become more involved in preventive oncology. "If John Yarbro (director of the centers program) insists that progress reports include prevention data, they'll soon get the message. NCI has to direct study sections to ask these questions. Prevention must become part of comprehensive centers."

The subcommittee agreed that its most important job was to convince NCAB members of the importance of prevention.

"They need to get religion," Nelson said. "Once they have the true faith, then we can get down to the specific missionary projects."

It's obvious that more evangelical work is needed if the subcommittee's views are to prevail.

TOXIC SUBSTANCES ACT WOULD BROADEN GOVT. POWER TO BAN CARCINOGENS

NCI's role as the only government agency conducting chemical carcinogenic tests on a systematic basis would change if Congress passes the Toxic Substances Control Act.

This measure (S.776), introduced by Sen. John Tunney (D-Calif.), would give the Environmental Protection Agency authority to require testing of suspected chemical substances, regulate their distribution and use and withhold them from distribution when the EPA administrator has reason to believe they would be a health threat.

The act would give EPA the power to ban or limit use of a chemical even without definitive data proving its carcinogenicity. Present law prohibits such regulation in the absence of scientific evidence that a substance can cause cancer in animals.

Language in the bill reads, "If warranted by data available to him, *or by the absence of data,* the EPA administrator may proposal a rule" limiting manufacture or distribution.

Testing (and the expense thereof) would be the responsibility of those who manufacture, import or process the chemicals.

The act would not be applicable to drugs, which are the regulatory responsibility of the Food & Drug Administration.

NCI tests from 150 to 200 chemicals a year in the bioassay program operated largely through a prime contractor, Tracor Jitco. Umberto Saffiotti, associate director for carcinogenesis in the Div. of Cause & Prevention, told the Subcommittee on Environmental Carcinogenesis that "a substantial number" of carcinogenic substances has been identified in the program. NCI follows up by notifying the appropriate federal agencies of the results.

NCI spends $35 million a year on the carcinogenesis program and has been criticized for not spending more. At a hearing on his bill, Tunney asked NCI Director Frank Rauscher why the budget did not reflect the importance of carcinogenesis studies, referring to a newspaper account that charged NCI was spending only 10% of its funds for such work.

Rauscher commented that the 10% figure was not accurate and that a variety of projects funded by grants and in the cancer control program fell into that category. Rauscher offered to provide Tunney with a list of those projects, and NCI staff is now combing the files for applicable grants and contracts.

Members of the Subcommittee on Environmental Carcinogenesis felt NCI should not become a "national testing agency" whatever the fate of Tunney's bill. Nor should it assume a regulatory function.

NCI's role should be a scientific one, the subcommittee agreed. It could monitor the quality of tests performed by other agencies or non-government organizations; coordinate the work of others, to help avoid duplication; should provide a "resource of the mind," Nelson commented; should have a strong role in the selection of chemicals to be tested and protocols to be used, subcommittee consultant Arthur McGee said; and should emphasize basic research and development of new test systems, Weinstein said.

"But we should always keep the option open for NCI to step in boldly when regulatory agencies may be too embarrassed to act," Nelson insisted.

The Tunney bill is given a better than even chance of making it through Congress this year or next, although possibly with some modifications. EPA Administrator Russell Train told Tunney that the Administration generally supports the bill, except for the provision that would require Se nate confirmation for an assistant administrator for toxic substance to be appointed by the President. The Administration also objects to the requirement that the budget for the program would be submitted by EPA directly to Congress at the same time it goes to the White House.

Tunney said he hopes to get the bill to the Senate floor within two weeks. The measure has not even started through the House, however. Paul Rogers, chairman of the House Health Subcommittee, undoubtedly will want to hold hearings on it.

BOARD, SCHMIDT CRITICIZE THE CRITICS FOR "IRRESPONSIBLE" ATTACKS ON NCP

Concern over the various expressions of criticism aimed at the National Cancer Program continue to occupy the attention of the National Cancer Advisory Board.

At the meeting this week, Board member Harold Amos, of Harvard, said he was worried that NCI was not doing an effective job of taking its story to the public. He questioned statistics used by writer Daniel Greenberg and his former colleague on the Board, James Watson, in attacks on the program (see following article by NCI Director Frank Rauscher).

Amos suggested that "we should find statisticians who don't have so many opinions" to develop data on survival rates.

"What we need is a statistician with imagination," Board Chairman Jonathan Rhoads commented.

Benno Schmidt, chairman of the President's Cancer Panel and a frequent antagonist of Watson when the Nobel Prize winner was on the Board, responded to news dispatches that quoted Watson as saying the cancer program was a "sham."

"I'm quite certain that the word Jim used wasn't 'sham'," Schmidt said. "We frequently heard him use another word, right here at this table, which he seemed to find more joyous.

"No one I know of, least of all Jim Watson, ever said that a cancer program commenced in 1972 was going to manifest itself in reduced death rates by 1975. For a scientist of Jim's caliber to make such a statement is evidence enough that he's engaging in demagoguery, and no amount of data will cure that.

"It is the knowledgeable scientists who are dissatisfied because certain things are not being done the way they want it done. It is members of the scientific community who are worried about us misleading Congress. The problem comes from people in our own ranks, who have been generously supported by us, and who have been listened to."

"And who don't know anything about clinical cancer," interjected Lee Clark, panel member and president of the Univ. of Texas System Cancer Center.

Board member Mary Lasker noted that progress made in treating childhood leukemia, Hodgkin's disease and Wilm's tumor is only now beginning to show up in national statistics. "We should publicize that," she said.

"Just what I was trying to say," Amos added.

Board member Denman Hammond agreed with Amos, that a systematic, regular effort to reach the public with the facts of the cancer program was needed to offset the criticism.

Board member Edward Burger said it was inevitable that expectations of early results would follow adoption of the cancer act, and that criticism of the program would ensure. "Greenberg's article was expected, but it was irresponsible," Burger said.

RAUSCHER RESPONDS TO CANCER PROGRAM CRITICISM BASED ON SURVIVAL FIGURES

NCI Director Frank Rauscher, pointing out that survival figures from the mid-1960s "obviously cannot be used to evaluate a program which became operational eight years later," has drafted a response to criticism of the National Cancer Program by science writer Daniel Greenberg.

Rauscher's article was inserted into the *Congressional Record* by Sen. Jacob Javits (R-N.Y.).

Rauscher's article follows in full:

THE NATIONAL CANCER PROGRAM: NOW THE GOOD NEWS

A recent article in the Washington Post entitled "Cancer: Now the Bad News:" which has appeared in Science and Government Report and the Columbia Journalism Review requires comment because it completely disregards the major accomplishments of the National Cancer Program.

The central theme of the article, by Mr. Daniel S. Greenberg, is that because 5-year survival figures published by NCI on patients who were treated from 1964 to 1969 showed only slight improvement in survival from many common forms of cancer, therefore, the National Cancer Program (NCP) enacted by Congress in 1971 was making little progress.

The fact is that increased funding for the NCP did not become available until 1972 and in 1973 the new NCI Cancer Control Program began its first year of operations designed to speed the application of the latest research results for the benefit of people. The full impact of this Congressionally mandated control program will not be felt for several years because it takes time to get the latest diagnostic and treatment methods into community practice where they may be applied for the benefit of all patients. It takes even longer to get knowledge about cancer prevention translated into public action. The Suregon General's Report identifying cigarette smoking as the major cause of lung cancer was published 11 years ago, yet lung cancer is now at epidemic proportions.

While Mr. Greenberg is correct in stating that survival from major forms of cancer did not improve dramatically between 1964 and 1969, obviously this cannot be used to evaluate a program which became operational 8 years later. Significant advance were, in fact, made in the 1960s and additional advances have been made since establishment of the national program.

Before discussing these advances, it is useful to examine the conceptual basis which is the foundation of our scientific effort to reduce and eventually eliminate deaths from cancer. The NCP plan, developed by more than 250 leading scientists and clinicians (most of them from outside the Federal Government) recognized that to reduce cancer mortality requires five things:

1. Finding causes in order to prevent the disease.
2. Early dectection and diagnosis because early disease is most successfully treatable.
3. Better treatment for early disease, since not all early disease is cured and too many patients go on to develop advanced disease.
4. Better treatment for advanced disease because people most often die of advanced disease.
5. Application of research findings for the benefit of people.

The research and outreach thrusts of the NCP are directed to all five of these necessary objectives: Uncovering the causes of the more than 100 forms of cancer will lead to prevention. Our programs in viral carcinogenesis, chemical carcinogenesis and epidemiology all search for cancer causes. We can take credit for having developed the sophisticated scientific techniques necessary to elucidate the role of viruses in human cancer and we can take credit for having recently isolated the strongest candidate to date for a human cancer virus. We have been able to identify chemicals and industrial pollutants that cause cancer and in some cases we have succeeded in identifying persons at high risk for developing cancer.

Some events are beyond our control or knowledge such as the sharp decline in the U.S. in the incidence of stomach cancer. We do not know why this is and we take no credit for it. A similar decline in the incidence and deaths due to cervical cancer can be largely credited to the development and application of better diagnostic methods.

Mr. Greenberg makes one reference to the fact that survival rates are not the only criteria for evaluating research in a field as complex as cancer, and the trend in cervical cancer is an excellent example of this. Survival had not improved in the 1969 figures because only women with more advanced disease were included. Those women with early

curable lesions, which would develop into widespread disease, were not included in the cervical cancer statistics. If they had been, survival would have shown a dramatic statistical improvement. This is just one example of how prevention, which is the best form of treatment, can be highly effective, yet the casual reader of survival statistics will conclude there has been no progress.

In the area of early detection and diagnosis, NCI and the American Cancer Society are now supporting 27 diagnostic centers to apply the techniques of early diagnosis that reduced breast cancer mortality by 30% among women screened by the Health Insurance Plan of New York. Approximately 250,000 women will be screened annually and we predict that this will yield a substantial saving in lives. Other projects in early diagnosis are under way for cervical and lung cancer.

Developments in early treatment include a report in recent months that adding a single chemical to the surgical treatment of breast cancer has substantially reduced recurrence of the disease.

Since advanced disease is the form of cancer that usually kills, it has been the focus of much of the research on treatment. In the last 15 to 20 years we have developed form sof systemic treatment that could be applied to patients with early cancer. These systemic treatments have been developed with advanced cancers such as the leukemias and lymphomas, which are usually widespread when discovered. Now that treating these disseminated diseases has been successful, we know that the same principles should be applicable both to other advanced cancer and to early cancers. Thus early and advanced breast cancer, and advanced ovarian cancer are now being treated with good results by the techniques that were developed over the years with leukemia and lymphoma. Today, the successful less disfiguring treatment of cancer is also a distinct possibility.

However, before better measures for prevention, diagnosis and treatment can be reflected in reduced mortality statistics, research findings must become common knowledge among both practicing physicians and the people. This is the mandate of the Cancer Control Program.

The concept of lag time is an important but poorly understood aspect of medical research. Perhaps this is because the American people have grown accustomed to rapid accomplishments such as the proof, in just two months of a summer in the early 1950s, that an effective polio vaccine was at hand. The scientific research leading up to these dramatic events required many years. 1969 survival figures cannot measure progress in the 1970s, but it is probably less obvious that they also barely reflect the effects of successful research programs—for example in the leukemias and lymphomas—that were introduced in 1963 and 1964. It will undoubtedly take several years for improved survival for specific cancer sites to be reflected in overall (or national) figures. For example, to test the effect of new treatment methods (such as new surgical techniques, new types of radiation, new chemotherapeutic agents, or a combination of these) usually takes a minimum of 3 to 5 years or more. Initial studies must be done on small numbers of individuals at selected institutions with particular expertise. After a new treatment has been evaluated, the next step requires dissemination of the new information and the adoption of the new methods by the medical profession for application to the population at large.

Thus, new treatment methods necessarily require 10 or more years to be reflected in overall survival figures. The fact that end result figures do not reflect what we know can be accomplished now at centers with special expertise in a given disease is all the more reason for a sustained national effort. Until passage of the National Cancer Act of 1971 the NCI had no mandate or specific funding for the translation of research results into widespread application—Cancer Control. Because of Congressional and Executive Branch initiatives the NCI now has a Cancer Control Program, but it is only in its second year of operation. Through a wide variety of agencies and voluntary organizations, it is setting up programs specifically designed to convert new research findings into widespread application as quickly as possible.

One example of our optimism both for new treatments that have been developed and for the human impact we can expect by applying these, is the 100% improvement in 50year disease free survival from all forms of childhood cancer treated since 1967 at M.D. Anderson Hospital and Tumor Institute, Houston, Texas.

In 1967 the number of children surviving five years without disease was 25% but by 1972 it was 50%. Obviously one of our goals is to save all of the roughly 7000 new cases of cancer which occur annually in the U.S. in children under the age of 15. However, saving 3500 children for 5 years is the equivalent of saving 17,500 years of life annually and 175,000 years of life-per decade.

Unfortunately, all of these children will not live to be 75, but if they did (and if their average age at treatment was 5 years) we would be preserving 245,000 years of life annually or 2,450,000 years of life over a decade. No one can responsibly dismiss savings of this human magnitude as statistically insignificant. Getting these improved treatments out to the American people, their doctors and community hospitals is a major goal of the Cancer Control Program.

Recent studies have also shown that 80% 2-year disease free survival from osteogenic sarcoma can now be achieved compared to 20% a few years ago. These 2-year data are encouraging because the disease was nearly always lethal within that time period.

Breast cancer is a major killer in which important progress has been made since the beginning of the NCP. Preliminary 2-year results indicate that a single drug (L-PAM) substantially reduces recurrences of disease and there are similar encouraging results in combination chemotherapy of advanced breast cancer. If these preliminary trends are sustained over a 5-year period the toll from this disease should be substantially reduced. Breast cancer is an instructive example of how therapeutic principles we have developed with less common advanced disease can be applied to major cancer killers.

The ability to cure and control 10 cancers has been developed since 1960. Even though these cancers account for only 8% of all cancer deaths per year in this country, these cancers are generally biologically virulent and frequently occur in young people causing a great emotional and economic impact and a staggering loss in years of life. For example, leukemia and lymphoma are often referred to as uncommon types of cancer, however, together in males they account for 360,976,000 person years of life lost. This is more than half of the loss caused by lung cancer, which is the leading killer of males. Leukemia, which accounts for one-sixth as many deaths as lung cancer in men, accounts for almost half as many work-years lost as lung cancer and is the second ranking cause of work-years lost for both men and women.

Thus, the ability to cure or control less common cancers may be far more important than incidence figures suggest. In 1960 survival from acute childhood lymphocytic leukemia was measured in months and less than 10% of patients with advanced Hodgkin's lymphoma survived for 5 years or more, and few if any of them were cured. Today, 5 year survivals without disease are reported for 51% of children with this form of acute leukemia at certain centers, and at other centers 5 year survival from advanced Hodgkin's disease has increased to approximately 70%. A substantial percentage of these patients are undoubtedly cured.

The key point to be made here is that these examples—and they are only a few of many—illustrate how we have built a scientific base with certain advanced cancers which enables us now to develop effective combined therapies for many other cancers, both early and advanced.

We have long recognized that since 1950 survival from cancer has continued to show a slow but steady improvement. The increase has not been as dramatic as increases between 1940 and 1950, but we have now built a rational scientific base which will exert an enormous impact on the cancer problem over the next decade. This is precisely the reason why we are conducting a broad-based program to improve on the four ways of reducing cancer mortality, which are prevention, early detection and diagnosis, and improved treatments for early and advanced disease. The application of our advances in all four of these areas through the Cancer Control Program will have a major impact over the years.

It should be noted that from 1950 to 1969 cancer mortality in the U.S. has decreased for women and increased for men. If cancers associated with smoking are removed from the overall statistics, cancer mortality has also decreased for men. Of 19 major forms of cancer reported in the recently published HEW document, "Cancer Rates and Risks," only three cancers—stomach, uterine cervix and pancreas—show no improvement in three-year survival after diagnosis and the incidence is declining for two of these cancers, stomach and uterine cervix.

Finally, it is well to remember that almost half of thecancer patients diagnosed in 1975 will not die of cancer and at least 3 million Americans who have had cancer are alive today.

SOLE SOURCE NEGOTIATIONS

Proposals listed here are for information purposes only. RFPs are not available.

Title: Administration and technical support services.

Contractor: Automation Industries, Inc.

Title: The 14th Annual Conference on Detection and Treatment of Early Breast Cancer

Contractor: American College of Radiology, Chicago.

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1-CP-55680-69

Title: *Feasibility study to define the modalities for a state of the art survey in diet, nutrition and cancer*

Deadline: *April 28*

The diet, nutrition and cancer program of NCI sponsors research and collects information on the role of diet and nutrition in the etiology of cancer, including determinants of susceptibility or resistance, and in the role of nutrition in the treatment, long-term management and rehabilitation of the cancer patient. The program also disseminates diet and nutrition information relative to the prevention, treatment, long-term management and rehabilitation of the cancer patient. The research efforts of this program are conducted by interested segments of the scientific community under either grant or contract funding.

NCI wishes to perform a feasibility study, the results of which will be later applied in determining the workscope of a future RFP to conduct a critical review of the current knowledge in the various relationships of diet and nutrition and cancer in establishing a continuing surveillance service of emerging scientific literature.

The contractor, under the direction of the NCI project officer and with the assistance of qualified consultants, will provide:

1. Definition of scientific literature sources in diet, nutrition and cancer.

2. Definition of a suitable classification of scientific publications to cover the etiologic, therapeutic and rehabilitation aspects of diet, nutrition and cancer.

3. Definition of criteria for determining the optimal depth of search in different areas of this literature review.

4. Definition of criteria for determining the reliability of individual research papers. This criteria should qualify a given work solely on the adequateness of experimental design, of materials and methods and of statistical evaluations.

5. Definition of criteria for condensation of information and format of annotated summary of current knowledge.

Upon completion of this task the contractor will submit a report indicating the definitions above, plus a critical analysis of costs and benefits expected in conducting the actual literature survey at different depths of detail. Submission of three or more options is expected.

It is expected that this project can be completed within 120 days after execution of the contract document. The contractor performing this feasibility study will be allowed to bid on an eventual future RFP for conducting the actual survey of scientific literature in diet, nutrition and cancer.

The approximate manpower requirements for this project are:

(a) Eight man months of professional time. Personnel qualifications will include relevant technological background and experience in this type of activity, and possibly an educational or experience background in nutrition and cancer; not necessarily at the doctoral level.

(b) Four man months of secretarial talent.

(c) Approximately 400 hours of expert consultants with relevant professional background in nutrition and cancer at the experimental and clinical levels. Selection of consultants will be made with the advice of NCI.

Contract Specialist: Linda Waring
Cause & Prevention
301-496-6361

CONTRACT AWARDS

Title: Breast cancer detection demonstration project
Contractor: Duke Univ., $176,667.

Title: Expansion of South Dakota cervical cancer screening program
Contractor: South Dakota Dept. of Health, $93,272

Title: Demonstration of cancer rehabilitation facilities and/or departments
Contractor: Memorial Hospital, NYC, $452,222.

The Cancer Newsletter—*Editor* JERRY D. BOYD

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