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HAS THE PENDULUM SWUNG TOO FAR TOWARD GRANTS? NCI, NCAB PONDER BEST WAY TO STIMULATE WORK IN NEW AREAS

NCI's attempt over the last three years to increase funds for research grants while cutting back on the size of its contracts budget has encountered a number of problems, not the least of which is the inability or reluctance of some study sections to consider new approaches and unfamiliar territory. (Continued to page 2)

In Brief

NCI CUTTING BACK SUPPORT FOR TRAINING MEDICAL, PEDIATRIC ONCOLOGISTS; CLARK RECEIVES ACS AWARD

NCI'S CLINICAL cancer education grants program was being discussed by the National Cancer Advisory Board. Maureen Henderson commented, "There are two points to consider. Are there too many medical oncologists? Do they make a lot of money?" William Powers added, "We need to know how many medical oncologists are practicing in this country." "If we have enough, we don't need to know how many," Henderson said. "This is coming out as it did with radiotherapists," said Powers, a radiotherapist himself. "There were too many being trained who were not trained well enough. Those coming out of this program are the best trained." Margaret Edwards, chief of NCI's Clinical Manpower Branch, said that the Clinical Cancer Education Review Committee is cutting back on the numbers of medical and pediatric oncologists being trained in the program. "They are beginning to be available in adequate numbers," she said. Noting that funds for clinical education have been reduced, Powers said, "We must preserve at least part of that program." NCAB Chairman Henry Pitot added, "When push comes to shove, I know the Board will want to keep it intact." . . . **R. LEE CLARK**, president emeritus of the Univ. of Texas System Cancer Center, has received the American Cancer Society Humanitarian Award "for his outstanding contributions as surgeon, cancer specialist, teacher and administrator, and especially for nurturing M.D. Anderson Hospital & Tumor Institute into the major comprehensive cancer center it is today." . . . **GERALD MURPHY**, director of Roswell Park Memorial Institute, has been elected national chairman of the ACS Medical & Scientific Committee. . . . **CONGRESS WAS** scheduled to adjourn at the end of this week, with extension of the continuing resolution one of the final items requiring action. The resolution provides interim financing for those agencies not funded yet through regular appropriations legislation, including NIH. The Senate Labor-HHS Appropriations Subcommittee, as one of departing Chairman Warren Magnuson's last efforts in his long history of supporting health research, planned to amend the continuing resolution to increase NIH funds, including $20 million more for NCI than approved by the House.

RFA PUT ON HOLD WHILE NCI CONSIDERS WHETHER CONTRACT WOULD BE BETTER

(Continued from page 1)

Grant applications in epidemiology, chemical carcinogenesis and clinical research invariably were scored low or disapproved by NIH Div. of Research Grants study sections, even before the new emphasis on grants. Pressures from NCI staff, the National Cancer Advisory Board, Congress and the scientific community resulted in establishing a new study section for carcinogenesis and agreement to set up ad hoc committees or add persons with appropriate expertise to existing study sections when required. Those improvements seem to have helped the situation.

Inadequate consideration of some grant applications by NCI's own review groups also has been a problem at times, but staff and NCAB members feel this might not always be corrected by adding expertise to those groups. The problem sometimes lies in the fact that investigators are encouraged to seek grant support in areas that are not well defined, and where there is little or no base of knowledge on which to build. They think work in those areas might better be supported with a mechanism which permits NCI to be more specific in describing the workscope—the contract mechanism. The pendulum, it seems, may have swung too far the other way.

An example which surfaced recently was the effort by the Div. of Cancer Control & Rehabilitation in 1978 to encourage submission of grant applications for community programs in cancer prevention. A request for applications (RFA) was published, describing NCI's interest and the general area it wanted to support. Forty-four applications were submitted, but a special review committee approved only 18, none with scores high enough to be funded at the established cutoff. The NCAB requested re-review, and eventually six were funded.

The Div. of Resources, Centers & Community Activities has since replaced DCCR, and earlier this year undertook plans to issue a new RFA for community response to specific carcinogenic hazards. But that RFA was put on hold after NCAB members recalled the previous difficulties and suggested that either the review committee be constituted with more appropriate expertise or that the program be switched to contracts.

"Basically it is a policy question," said Andrew Hegyeli, program director for carcinogenesis in DRCCA. "We don't know the best way to stimulate this area. In an area where the expertise is already developed, an RFA is probably the best approach. Many areas of public health are not well defined, and RFPs (request for proposal for contracts) might be better."

Hegyeli said, "I personally feel the best approach" for supporting the community response to carcinogenesis hazards problem would be through state health departments.

The issue may be presented to the DRCCA Board of Scientific Counselors at its January meeting. It is possible that lack of funds will preclude any additional projects in this particular field, but the policy question will remain: When should the determination to encourage investigators to seek grants be relaxed in favor of more tightly defined contract supported work?

The six existing grants in the area are:

- Cancer in women receiving exogenous estrogen, Univ. of Denver, Mary Arnold, principal investigator. Objective is to demonstrate a model surveillance and followup system for postmenopausal women taking hormones.
- Community based intervention for high risk workers, Workers Institute for Safety & Health, Knut Ringen, PI. Objective is to develop a program of cancer prevention and intervention for cohorts of workers and their families identified at high risk of cancer due to workplace exposure to hazardous agents.
- Education approaches to endometrial cancer control, New York State Dept. of Health, Susan Standfast, PI. Objective is to increase knowledge and motivate changes in practice toward reduction of incidence for uterine cancer through education of women, physicians and nurses on risk factors from use of estrogen and earlier recognition of vaginal bleeding as a symptom of cancer.
- Cancer prevention is your choice, Fred Hutchinson Cancer Research Center, G. Hongladarom, PI. Objective is to teach school children, school personnel, parents and community organizations about cancer prevention, leading to a comprehensive statewide plan for cancer education.
- Environmental cancer prevention and labor health education, Johns Hopkins Univ., Virginia Wang, PI. Objectives are the development of a relevant health education model for college bound industrial workers with the expectation that they will impact on coworkers, management and the community; and identification of mechanisms and linkages by which cancer prevention information can be disseminated to workers.
- Development of protocols for worker notification, Western Institute for Occupational and Environmental Sciences Inc., P.L. Polakoff, PI. Objective is to identify labor union communication channels to provide notification and information to workers about exposure to carcinogens in the workplace.

SMOKING/HEALTH PROGRAM TRIES GRANTS, LEAVES DOOR OPEN FOR CONTRACT USE

Another area in which NCI is attempting to encourage investigator initiated research is the Smoking,

Cancer & Health Program. The jury is still out on that effort, and NCI still could find that it will have to rely on contracts for the bulk of the work.

A program announcement was issued in January of this year, expressing NCI's interest in receiving grant applications in basic and applied studies in toxicology, epidemiology, prevention, behavior, attitudes, pharmacology, education, information, training and other appropriate areas related to smoking and health.

"The program originally relied entirely on contracts," said Diane Fink, who heads the program. "We wanted to let investigators know that grants were available and that we did want to support investigator initiated work. Where it is appropriate, we will still use contracts."

A program announcement differs from a request for applications in that an RFA stipulates that a certain sum of money has been set aside to fund those grants, while a program announcement does not.

NCI staff does not yet have a handle on the response to the program announcement or how those responses fared in review. They are reviewed by NIH Div. of Research Grants study sections, and some may be assigned to other institutes. Only those making the March 1 deadline have been awarded to date, and that probably was too soon to have stirred up much response.

"It's hard to draw a conclusion now," Fink said. "The July deadline was more realistic." Those will be awarded following the January-February meetings of the National Cancer Advisory Board and other NIH institute councils.

Fink is chairman of the Interagency Group on Smoking & Behavior, which is attempting to coordinate smoking related research, education and demonstration activities throughout the Dept. of Health & Human Services. NCI and the National Heart, Lung & Blood Institute support most of the work in the Public Health Service, $13.2 million for NCI in the 1980 fiscal year, $11 million for NHLBI. The National Institute of Child Health & Human Development had $4 million, and National Institute of Environmental Health Sciences $1.2 million, for a total of $29.4 million at NIH.

The Alcohol, Drug Abuse & Mental Health Administration (ADAMHA) had $2.4 million in smoking projects in 1980, through its National Institute of Drug Abuse. The Center for Disease Control supported $13.5 million in education demonstration projects, the National Institute of Occupational Safety & Health had $800,000 in worker related projects, and the assistant secretary for health office had $2.5 million for various activities including advertising and operation of a clearinghouse.

Fink acknowledged "there is a big potential for duplication" of NIH's grants by ADAMHA and NIDA. This is controlled to a large extent by the fact that the NIH's DRG assigns NIDA's grants. DRG also may refer grants to ADAMHA and to NIOSH when appropriate. The Interagency Group meets regularly with DRG staff to help sort out grant applications. Letters of intent requested in the program announcement are circulated to all participating agencies. So far, there are not so many applications that it has been difficult to manage, Fink said.

In the 1980 fiscal year, NCI supported $2.8 million in smoking and health related grants, $9.6 million in contracts, and $865,000 in intramural work. The estimate for 1981 is $5.8 million in grants, $6.4 million in contracts and $1 million intramural.

Fink and other NCI staff members reviewed the Smoking, Cancer & Health Program for the NCAB last month. The program was started in the early 1970s and emphasized development of a less hazardous cigarette through reduction in tar and nicotine content. Its primary advisory body was the Tobacco Working Group which included representatives of the tobacco industry. Much of the work was done through subcontracts with a prime contractor. Emphasis now has been changed, dropping the less hazardous cigarette work and phasing out the prime contract.

NCI Director Vincent DeVita told the NCAB that work on less hazardous cigarettes was dropped because of budget restrictions and because "we felt that product development is the job of industry," although investigator initiated grants along those lines still might be supported by NCI. The institute also still is interested in supporting epidemiology studies of the effects of different types of cigarettes, DeVita said.

NCAB member Philippe Shubik noted that he had been a member of the Tobacco Working Group. "I was totally opposed to the safe cigarette program initially," he said, "but I came to think that it was productive. It is a program in which NCI took a big lead, and can point to with pride. (E. Cuyler) Hammond (of the American Cancer Society) and others seem to feel that the low tar and nicotine cigarettes are making a difference. It is quite a success for the Cancer Institute."

NCAB member Irving Selikoff commented that he had also been a member of the Tobacco Working Group. "The industry representatives played it close to the vest. Most of the information we got came from the (U.S.) Dept. of Agriculture. I could hardly believe my ears when some members said that the NCAB should not have any control over the program, since the only ones in the world who knew anything about tobacco research were in that room. I did not think it was appropriate for industry to be on that group."

Shubik said that Selikoff had been a member of the group in its earlier stages and that he, Shubik, had seen it at work later when industry representa-

tives had made significant contributions.

"What was the impact of the NCI program on industry's development of the low tar brands?" NCAB member Sheldon Samuels asked.

Shubik said there "is no question" that NCI's contribution was significant. "It had a major impact."

John Pinney, of the Office of Smoking & Health, said that industry claims to have invested $15 billion in producing the low tar and nicotine brands. "I suspect we would have had that development without NCI's program. Whether it was faster or slower, I can't say."

Pinney said the decision to move from less hazardous cigarette design to studies to determine what effects they have had was made by the surgeon general in 1979. "Industry has gone as far as it can in reducing tar content," he said. There are brands now with as little as .01 mg of tar. The average now is 17 mg, while a plethora of brands in the 2 mg to 10 mg range are on the market. Prior to 1960, the average tar content was 40-50 mg per cigarette.

A few brands with less than 10 mg were on the market for years but were unacceptable to most smokers because they lacked the flavor of the higher tar brands. In the mid 1970s, with impetus from NCI's program stimulating interest in development of less hazardous cigarettes, the tobacco industry began marketing brands with markedly reduced tar and nicotine content and with flavor additives. These brands now account for about 50 percent of the total market today.

"Do you know what is in the additives?" Selikoff asked.

"They are considered trade secrets," Pinney said. "We have no authority to require them to reveal that information, but we are negotiating with industry."

John Holbrook, assistant professor of internal medicine at the Univ. of Utah, has been conducting a survey of U.S. smoking habits. He told the NCAB that "sometimes people do not know how well their programs are succeeding." Smoking cessation efforts by the American Cancer Society, by NCI's Office of Cancer Communications and others have contributed to a sharp drop in the number of males over age 40 who smoke.

Holbrook said the ACS study found that with a 50 percent reduction in tar, a 15 percent reduction in risk of cancer resulted, suggesting that "there may be something else in the smoke."

"Is it possible that in the process of removing the tars some anticancer agents are also removed?" NCAB member Harold Amos asked. Holbrook did not know the answer.

"The rising rate of lung cancer in women is alarming at a time when the 'safe' cigarette is in vogue," DeVita said. "When I stopped smoking in 1967, I had been smoking low tar brands."

"Low tar then is high tar now," Holbrook said. Women who are getting lung cancer now probably started smoking in 1945-50.

Selikoff said that the ACS study, which indicated there was only a 15 percent decrease in risk with a 50 percent decrease in tars, primarily dealt with a population which began smoking before 1960. "They are now smoking low tar and nicotine brands, but they smoked others before switching."

Nevertheless, NCAB member Maureen Henderson said, "people who don't smoke at all don't get a wide range of disease. 'Safe' cigarette is not a proper term."

"It's safer," DeVita said. "Safer than walking across the street with your eyes closed."

A research conference on the low yield cigarette held last summer developed suggestions for a wide variety of studies which the Smoking, Cancer & Health Program could support.

Fink said NCI presently is considering some of the suggestions for possible RFAs and RFPs, and other agencies similarly are sifting through them. These, developed by a series of working groups, included:

Behavioral Aspects Working Group

1. Controlled pharmacologic studies, in both the animal and the human, to determine the role of nicotine as the primary reinforcer in cigarette smoking, its role in self-administration, tolerance, and physical dependence. Research has been slowed by the lack of standardized test materials and accessible laboratory analyses.

2. Prospective studies of compensatory smoking behavior, in both voluntary and experimental switching models, measuring the frequency and extent of changes with various tar and nicotine contents, including measures of satisfaction.

3. Studies to characterize the natural history of cigarette smoking and the role of reduced-yield cigarettes at critical transition points in a smoker's history, including initiation, maintenance, cessation and relapse.

4. Establishment of central clinical testing facilities for assays of serum nicotine, cotinine, blood carboxyhemoglobin and saliva thiocyanate.

5. Development of clinically acceptable cigarettes which independently vary yields of nicotine, tar and carbon monoxide.

6. Development and validation of standardized smoking machine yield measurements of tar and nicotine which closely reflect the pattern of human cigarrete smoking, to provide better information to the consumer and to the researcher.

Cancer Working Group

1. Expansion of retrospective and longterm prospective epidemiologic studies on all tobacco related diseases, and with specific reference to brand of cigarettes smoked, number of cigarettes, manner of smoking, inhalation, etc., and especially studies of high-risk occupations and groups.

2. The development of institutes or multidiscipli-

nary centers where basic scientists, physicians, epidemiologists, statisticians, social scientists and related experts concerned with the smoking and health problem collaborate.

3. Relative to carcinogenesis, additional work on the effects of nitrosamines, tobacco flavoring agents and additives, tar, gaseous phase of cigarette smoke, additive, synergistic, or antagonistic effects of various smoke constituents in carcinogenesis, acrolein, and anticarcinogens, or preventive compounds such as vitamin A or retinoids.

4. Continuation of the cooperative international epidemiologic studies of the tobacco related cancers.

5. Research on identification of groups at high risk of developing tobacco related disease, possibly by genetic markers, such as HLA.

Pharmacology/Toxicology Working Group

1. Routine and frequent surveillance of current cigarettes for:

—Specific chemical constituents, including nicotine, benz(a)pyrene, phenols, catechols, nitrosamines, carbon monoxide, hydrogen cyanide, nitrogen oxides, aldehydes and radionuclides.

—Biological activity, i.e., sebaceous gland assay, mutagenesis assay, airway effects, ciliotoxicity, and urine metabolite measures.

2. Determination of parameters of smoke intake by cigarette smokers including puff volume, puff duration, puff frequency and inhalation profiles by type of cigarette.

3. Evaluation of the pharmacodynamics and etiologic roles of nitrosamines, specific to tobacco smoke; nicotine, and other alkaloids.

4. Systematic investigation of the effects of varying smoking machine parameters on the relative and absolute yield measurements.

5. Determination of the influence of raw product modification, including genetic manipulation, curing practices, fertilization and the use of pesticides on health-related parameters.

6. Characterization of the physical and chemical properties of mainstream and sidestream smoke from cigarettes delivering less than 10 milligrams of tar.

7. Development, validation and standardization of analytical methods for smoke constituents.

SOLOMON GARB'S QUESTIONS AND ANSWERS ABOUT THE NATIONAL CANCER PROGRAM

Solomon Garb, who as chairman of the Citizens' Committee for the Conquest of Cancer has spent much of the last 10 years explaining and defending the National Cancer Program, has compiled a list of questions he is frequently asked and the answers he gives.

These questions and answers may be useful to others who serve as advocates of the program from time to time, so ***The Cancer Letter*** will publish the compilation during the next few weeks. Those who wish to do so may photocopy, without further authorization from ***The Cancer Letter,*** the questions and answers for distribution as they see fit.

Garb presently is recovering from cancer surgery at M.D. Anderson Hospital (***The Cancer Letter,*** Nov. 28).

QUESTIONS ABOUT THE NATIONAL CANCER PROGRAM

These questions and answers are presented by the Citizens' Committee for the Conquest of Cancer. They are designed to give factual information about the progress of the National Cancer Program and about future needs.

The National Cancer Program was given a new impetus by the Cancer Act of 1971 which provided for the National Cancer Institute a substantial degree of freedom from its superior government agencies, the National Institutes of Health and the Dept. of Health, Education & Welfare (now Health & Human Services). In addition, there was increased funding through 1975, but since then, the increases have not kept up with inflation, and the program is seriously underfunded.

The National Cancer Program has been questioned and criticized. We are presenting our answers to the major questions and criticisms. Some of the questioners were hostile, but many just wanted information. We have condensed some of the questions, but believe that we have preserved their intent. Occasionally, questions overlap two areas or a logical sequence of questions covers several areas so that a small amount of repetition may be found.

CANCER TREATMENT AND TREATMENT RESEARCH

1. What good has the Cancer Program accomplished?

It is in cancer treatment that the greatest gains have been achieved. Here are some examples.

A. Acute lymphocytic leukemia of children was once 100 percent fatal. Now more than 50 percent of those who are properly treated will be cured. Some of the earlier cured children have now grown up, married and had healthy normal children of their own.

B. Primary bone sarcoma had only a 20 percent survival rate in two years. Now, the two year survival rate is over 65 percent and we believe most will be full cures.

C. In Hodgkins lymphoma, which used to kill all victims, we are now achieving over 70 percent cure rates. We hope to do better.

D. In several other types of cancer of children and young adults which used to have extremely low cure rates, we are now curing over 50 percent. These include choriocarcinoma, rhabdomyosarcoma, retinoblastoma, early Burkitt's lymphoma and Wilms' tumor.

E. In cancer of the testis, a dramatic advance is now in progress. In the past it was possible by prompt surgery to cure early cases in which there was no spread. However, once the cancer had spread to other organs, no cures were possible—before the Cancer Act of 1971. Today, even after gross visible spread to other organs such as the lung, over 50 percent of patients with metastatic cancer of the testis have no evidence of disease two and a half years after treatment. We believe that most of them will be permanently cured, but will have to wait several more years to be sure.

F. In breast cancer, we have learned that a Halsted radical mastectomy is not needed. Each year, this is sparing tens of thousands of American women an unnecessarily mutilating and disabling operation. In addition, in premenopausal women adjuvant chemotherapy is reducing the recurrence rate by about two thirds.

There are less dramatic advances in other cancers. We don't have enough government support to move ahead rapidly on all

of the 100 fronts that comprise the battle against cancer.

There have also been important advances in basic research and in diagnosis. However, the nature of these advances does not permit early evaluation of this eventual importance.

2. Why hasn't progress been faster?

A. Cancer is a complex of over 100 diseases and the most difficult problem ever tackled by medical research. B. The National Cancer Institute has never received the full appropriation needed. Each year, it has received about 40 percent less than was recommended by the nation's cancer experts. C. The National Cancer Institute must abide by all government rules and regulations, some of which slow things down without helping any patients.

3. Are any cancers really cured?

Absolutely. We define "cure" as a result in which there is no evidence of disease, at least five years after treatment. By that definition we are now curing between 500 and 600 Americans of cancer every day. This doesn't include skin cancer where the cure rates are well over 90 percent.

4. In general, though, is it a good idea to try to develop or improve treatments before the fundamental scientific research on a disease has reached the stage from which a logical treatment approach can be developed?

It is from the point of view of a patient who is doomed to die before the fundamental scientific research can provide a treatment and for those who care for that patient.

5. Has it ever happened that successful prevention or treatments of serious diseases were developed before fundamental scientific research showed a logical way to proceed?

Many times. The use of quinine to control malaria came many hundreds of years before there was any fundamental research on malaria. Smallpox vaccination was in use almost 200 years before fundamental scientific research revealed the cause of smallpox. The use of digitalis glycosides to treat congestive heart failure started more than 200 years before there was any fundamental sceintific research to explain it. Prevention of scurvy was described almost 200 years before vitamin C was identified. Opium derivatives such as morphine and codeine, were providing relief from pain many decades before fundamental scientific research gave even a hint of how and why they work. Fundamental scientific research has still not told us how aspirin relieves headaches. Other examples of treatments that helped patients without waiting for fundamental scientific research include quinidine for cardiac arrhythmias, ether for anesthesia, ergot alkaloids for use in childbirth, several medications for parasite infestations, and others.

6. Does that mean that fundamental scientific research is not important?

Not at all. Some treatments have come from fundamental scientific research and more may do so in the future. We fully support fundamental scientific research, but we will not let patients die without trying to help them. We believe it is reasonable to use some of the funds that the Congress has appropriated to try to help patients who have cancer now.

7. Have you cured or controlled any cancers before the fundamental research on those cancers was essentially completed?

Yes. Successful treatment of all the cancers in question 1 is saving the lives of scores of patients every day, even though the fundamental research is far from complete.

8. Aren't most anticancer drugs toxic?

Yes.

9. Is anything being done to reduce the toxicity?

Yes.

A. Studies in progress already suggest that for some anticancer drugs, toxicity can be reduced and efficacy increased through giving the drugs by continuous intravenous infusion for a period of hours or even days.

B. Studies are in progress on ways to prevent all or most of the nausea and vomiting caused by treatment and have shown early success.

C. There are plans for a major research effort to develop the second generation of anticancer drugs—medicines that would be substantially more effective and less toxic than those now available. Thus far, because of inadequate funding, this program is just inching ahead, but when funding is adequate it can pick up speed. Still, we cannot expect much in the way of reported statistical results for six to seven years after this part of the program moves into higher gear, since it takes that long for new drugs to be fully tested.

10. Has cancer research found treatments for diseases other than cancer?

Yes. Those diseases fall into the general classification of autoimmune diseases—conditions in which the body defenses become confused and attack normal cells. Some of these autoimmune diseases can be treated by corticosteroids. However, when that treatment fails, the anticancer drugs may be lifesaving. The diseases that are sometimes controllable by anticancer drugs include Behcets disease, Crohn's disease, dermatomyositis, erythroid aplasia, Goodpasture's syndrome, hemolytic anemia, hyperglobulinemic purpura, keratitis sicca, lupus erythematosus, pemphigus, periarteritis nodosa of the kidney, polyneuropathy, pyoderma gangrenosum, Reiter's syndrome, sympathetic ophthalmia, thrombocytopenic purpura refractory, and Wegner's granulomatosis. These are rather rare diseases, but generally serious and often fatal without treatment.

11. What about the costs of treatment research?

Please see the section on costs and finances.

12. Why are there anticancer drugs that are not available to all cancer specialists, but only to a limited number?

Because government regulations require extensive testing before a drug can be released for general clinical use. This testing is done at a few institutions.

13. Is there any way that any of the investigational medications can be obtained for a patient who is not in one of the special institutions?

Sometimes, The regulations are complex, and change from time to time. It is best if the physician seeks advice and guidance directly from FDA or NCI.

14. Which anticancer drugs can be used in most hospitals?

Adriamycin (doxorubicin), aspartase, azathioprine, BCNU, bleomycin, busulfan, calusterone, CCNU (lomustine), chlorambucil, cis-platinum, cyclophosphamide, cytarabine, dacarbazine (DTIC), dactinomycin (actinomycin D), floxuridine (FUDR), fluorouracil (5FU), hydroxyurea, mechlorethamine (nitrogen mustard), megestrol (megace), melphalan, mercaptopurine, methotrexate, mithramycin, mitomycin, mitotane, pipobroman, procarbazine, tamoxifen, testolactone, thioguanine, thiotepa, uracil mustard, vinblastine, vincristine. In addition to these some other drugs have several names. In round numbers, there are 35 to 40 drugs now available to treat cancer.

15. With that number, why can't you cure more cancers?

Cancer is not one disease, but over a hundred. Ordinarily, it takes a combination of three to four drugs to cure those cancers that can be cured by drugs.

16. Does that mean that you will need 300 to 400 drugs eventually to cure all or most cancers?

Not necessarily. The second generation anticancer drugs should be more effective. The third generation, which at present rates of progress should start becoming available around 1995 would be still more effective.

17. How many new anticancer drugs are now in clinical trials but not yet available for general use?

Approximately 50 to 55 not counting those which are currently being dropped for excessive toxicity or ineffectiveness.

18. Of those 50 to 55 new drugs, how many are likely to be effective enough for general use?

Based on past experience, we estimate that about 15 to 20 will be in general use and three to six will be major, lifesaving additions.

19. How long will that take?

Some will be available in a year, others in two to five years.

20. Why so long?

It takes a long time to do all the studies required by regulations and the funds available are limited.

21. How many of these new drugs would you consider to be second generation?

About three or four.

22. Can't something be done to speed up the process?

Yes, but it would cost far more money than NCI has available.

23. After a new drug is found to work on animals with cancer, how long does it take before it can be given to patients?

Six to eight years. The delay used to be seven to 13 years.

24. Why?

We can't be certain. Some claim that government regulations are excessive. Others claim that the research itself takes a long time.

25. Why do cancer scientists keep looking for a single cure for cancer when, in fact, cancer is 100 or more different diseases?

This question probably arises from erroneous stories which have appeared in several large newspapers. The truth is that almost all cancer scientists are convinced that many kinds of treatment will be needed before we know how to cure all cancers. The report of the National Panel of Consultants on the Conquest of Cancer told the Senate in 1971 that, "It is erroneous to think of cancer as a single disease with a single cause that will be subject to a single form of immunization (as in the case of polio) or a single cure. Cancer comprises many diseases...and will have to be dealt with in a variety of ways." Congress understood that when it passed the National Cancer Act in 1971.

26. What is being done to relieve cancer patients of the terrible nausea and vomiting that accompany chemotherapy?

Clinical studies are in progress in at least eight institutions to prevent or reduce nausea and vomiting from chemotherapy. These studies are coordinated by NCI. There has already been substantial progress. In one institution, the degree of nausea and vomiting has already been reduced by about 75 percent by the use of tetrahydrocannabinol (THC).

27. How can I find out the name of the nearest hospital that has THC available?

Write to the Div. of Cancer Treatment, National Cancer Institute, Bethesda, Md. 20205, or to Citizens' Committee for the Conquest of Cancer, 7159 South Franklin Way, Littleton, Colo. 80122.

28. Why is there a controversy over whether the cancer program is curing or controlling more cancers?

Those who go by statistics that are six or more years outdated see little or no evidence of progress. Those who see cancer patients every day see encouraging progress.

29. Can you estimate how many lives have been saved by the National Cancer Program that would not have been saved if there had not been such a program?

It's difficult to be certain. Some patients who had widespread cancer three years ago now seem well, but we won't know for two more years if they were probably cured or just given a few extra years. A recent estimate is that we are saving an extra 11,000 per year.

30. Are those patients really cured, or will their cancers return?

No one can be certain. However, the best estimate of clinical cancer experts is that they are actually cured. In some cases, children who had acute lymphocytic leukemia that used to be 100 percent fatal, recovered after therapy, grew up, married and now have normal healthy children of their own. We think they are cured.

31. What is the difference between treatment research, treatment related research, and basic research, and what percentage of NCI funds go to each?

Treatment research, also referred to as clinical trials is the study of new treatments and combinations of treatments on patients who volunteer for such studies. This takes up about 10 percent of the NCI budget.

Treatment related research is not done on patients but bears a direct and clear relationship to possible future clinical trials or clinical use. Examples are testing experimental treatments on mice, or on cells in tissue culture, or finding ways to produce and purify interferon for future clinical trials, or searching for new anticancer medicines in plants and microbial products. An intelligent layperson can readily see the direct relationship between this kind of research and possible clinical use. This type of research takes about 12 to 17 percent of the NCI budget. Altogether, treatment research and treatment related research account for about 28 percent of the NCI budget.

Basic research does not bear any direct, obvious relationship to clinical problems. However, the hope is that it would eventually lead to a broader understanding of the ways in which cells function. Examples are studies on DNA or on enzymes within cells. Basic research received about 53 percent of the NCI budget.

32. Are there any promising investigational treatments that are not progressing rapidly because of insufficient funds?

Yes. From June 19 to 21, 1979, a House committee under the chairmanship of Congressman Claude Pepper held extensive hearings on the progress of the clinical cancer program. They heard over 30 witnesses. All agreed that in general, there had been excellent progress since the passage of the Cancer Act of 1971. However, they reported at least six major areas in which progress was slowed because of inadequate funding.

33. How qualified were those witnesses?

They included the most distinguished and experienced clinical cancer specialists in the nation. Almost all are or were professors at outstanding medical schools.

34. Apparently some professors support the Cancer Program and others oppose it?

Yes.

35. Can you explain why?

We have observed that the professors who treat many cancer patients are overwhelmingly in favor of the Cancer Program. We have also observed that usually the professors who oppose it either treat no cancer patients or hardly any.

36. Is it possible to cure or control any cancer after it has spread?

Yes, largely because of the improvements brought about through the National Cancer Program. The numbers of patients whose cancers are cured or controlled after spread to distant organs is still small. However, those numbers are growing steadily. Mainly, we have obtained dramatic improvements in the outlook for testicular cancers, Hodgkins' lymphoma, and a few breast cancers. It is now clear that distant spread of cancer need not always be a hopeless situation.

37. Where do anticancer medications come from?

Chemical synthesis, microbial organisms (antibiotics and other products), higher plants, human blood (interferon), and, possibly in the future, from human cells grown in culture.

38. Are there other improvements that could be made to speed the development of more effective, less toxic anticancer drugs?

Yes. Each comprehensive cancer center and some of the smaller centers could be asked to develop programs to find new and better anticancer drugs. They could be given startup grants of about $3 million each to begin the process.

PROGRAM ANNOUNCEMENT

Cancer Clinical Treatment Research

NCI's Div. of Cancer Treatment desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the clinical treatment of cancer. Appropriate studies include the elucidation of the effects of various treatments and related tissue responses, toxicology and the importance of host factors in disease occurrence, rate of progression and curability. Improved experimental design, data management, statistical analysis, as well as specific experimental developments in supportive care methods and modalities are integral aspects of this program. Applications dealing with innovative approaches in surgical oncology are of particular interest. In making this program announcement, it is not the intent of the National Cancer Institute to make or imply any delimitation related to cancer clinical treatment research, but rather to stimulate investigator-initiated research in clinical treatment.

Applications in response to this announcement will be reviewed on a nationwide basis in competition with each other, and in accord with the usual peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of nonfederal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

Applications should be submitted on form PHS 398, which is available in the business or grants and contracts office at most academic and research institutions or from the Div. of Research Grants, NIH. The phrase, "Prepared in response to program announcement on Cancer Clinical Treatment Research" should be typed across the top of the first page of the application. Additionally a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement.

Applications will be accepted in accordance with the usual NIH receipt dates for new applications: March 1, July 1, Nov. 1. The original and six copies of the application should be sent or delivered to: Applications Receipt Office, Div. of Research Grants, NIH, Westwood Bldg. Room 240, Bethesda, Md. 20205.

For further information, investigators are encouraged to contact: Dr. William DeWys, Program Director for Clinical Treatment Grants, Landow Bldg. Room 8C17, Bethesda, Md. 20205, phone 301-496-4844.

In order to alert DCT to the submission of the proposals with primary thrust directed to clinical treatment research, a copy of the covering letter should be sent under separate cover to DeWys.

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 Contracting Officer or Contract Specialist named, Research Contracts Branch, National Cancer Institute, Blair Building, 8300 Colesville Rd., 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-CP-15733-74

Title: *Statistical analysis of bioassay data*
Deadline: *Jan. 26*
TOTAL SMALL BUSINESS SET-ASIDE

The National Toxicology Program is interested in receiving proposals that will propose to provide statistical and computational expertise and resources to summarize, analyze, and aid in the interpretation of data from the NTP bioassays. NTP estimates that this project will require 20 man-years of effort over the five year period.

Contract Specialist: Odessa Henderson
Carcinogenesis
301-427-8764

RFP AMENDMENT

RFP N01-CM-05720-57

Title: *Preclinical canine bone marrow transplantation*
Deadline Change: *To Jan. 9*

This RFP was publicized on Sept. 4, 1980. The deadline for submission of proposals is extended to Jan. 9, 1981 due to changes in the statement of work and level of effort required. It is anticipated that the project will require approximately three technical and support labor years of effort.

Contracting Officer: Damian Crane
Cancer Treatment
301-427-8737

The Cancer Letter _Editor Jerry D. Boyd

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