January 1 to December 31, 1986

President's Cancer Panel

Report of the Chairman

U.S. Department of Health and Human Services

Public Health Service

National Institutes of Health

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President's Cancer Panel

National Cancer Program National Cancer Institute

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March 9, 1987

The President
The White House
1600 Pennsylvania Avenue
Washington, DC 20500

Dear Mr. President:

Once again it is my duty, as Chairman of your Cancer Panel, to report to you on the status of the National Cancer Program as operated by the National Cancer Institute (NCI). The enclosed report represents also the efforts of my fellow Panel Members, Dr. William P. Longmire, Jr. and Dr. John A. Montgomery. We have been ably served in this task by Dr. Elliott H. Stonehill, Assistant Director of the National Cancer Institute, who serves as Executive Secretary of the Panel. We are also grateful to the distinguished Director of the NCI, Dr. Vincent T. DeVita, Jr. and other members of his staff for their assistance and cooperation.

Briefly, I would like to point out some salient points in the report.

This has been a year of significant advancement in a number of important areas in that new methods for improved therapy of cancer patients have been developed, the survival of treated cancer patients has increased, and new approaches to promote cancer prevention have been implemented.

Of particular interest is the protocol using lymphokine-activated killer (LAK) cells and interleukin-2 (IL-2). Work has continued in this important area first reported to you in 1985. Clinical studies involving IL-2 are being intensively pursued in many hospitals and cancer centers throughout the country. There have been encouraging, positive results with this new treatment, and with additional research and continued clinical trials, there is every reason to believe that even more positive results will be achieved in the future. At a recent workshop I sponsored at the Salk Institute in La Jolla, California, representatives of the organizations which are pursuing the LAK-IL-2 trials met, and it was clear that those distinguished scientists believed we were dealing with a significant new treatment with definite potential for anti-tumor activity. I predict the next year will see even greater improvements in this new protocol, making it one of the most significant tools we have at our disposal in the fight against cancer.

The acquired immune deficiency syndrome (AIDS) continues to be a serious problem facing the country, but the NCI has been very active in developing drugs for treatment and research into a vaccine. Progress is continuing in both areas.

Finally, more attention is being given to the prevention and control of cancer, and these efforts are important and deserve support.

Our conclusion is that while we are making progress, much more remains to be done. The goal we pursue is tremendously important — the removal of cancer from its preeminent position as the most dreaded of diseases afflicting mankind. We cannot achieve that goal without continued and increased Federal support for the National Cancer Institute. We urge you to provide that support for the benefit of cancer patients and potential victims and their families who look to us for help.

Mr. President, it is a privilege to serve you as Chairman of your Cancer Panel. I hope the attached report will prove useful to you and others in your Administration. As always, I stand ready to be of any assistance possible to you and your colleagues as you face the great challenges that lie ahead.

With warmest regards,

Respectfully,

Armand Hammer

Dr. Armand Hammer
Chairman

1986 CHAIRMAN'S REPORT TO THE PRESIDENT

This has been a year of significant advancement with exciting new research discoveries in a number of important areas of the National Cancer Program. New methods for improved therapy of cancer patients have been developed, the survival of treated cancer patients has increased, and new approaches to promote cancer prevention have been implemented. This report will briefly summarize the progress witnessed this year which provokes strong optimism in the long crusade against cancer.

During 1986 the President's Cancer Panel held four meetings at centers of research excellence in the Nation. We heard reports which detailed the progress being achieved in cancer treatment, advances which evolved from research programs supported by the National Cancer Institute (NCI).

Panel meetings were held in Los Angeles, Memphis, Boston, and Chicago. In each city, we discussed innovative approaches to cancer therapy, including reviews of regional progress and in-depth analyses of the National approach to specific new therapies.

My colleagues on the Panel, Dr. William P. Longmire, Jr. and Dr. John A. Montgomery, and I, together with Dr. Vincent T. DeVita, Jr., Director of the NCI, heard reports at our meetings of significant advances in the use of immunologic and genetic methods for treatment, as well as the promise of new potential cures for some forms of cancer which had not previously been tractable.

The Panel also actively participates in all meetings of the National Cancer Advisory Board, and thus is able to appraise all aspects of the NCI responsibilities which are explored in detail at those sessions.

Cancer Treatment

The immunotherapeutic attack on cancer cells, using lymphokine-activated killer (LAK) cells and interleukin-2 (IL-2), was vigorously studied in a number of clinical research centers this year, following the leads established by Dr. Steven A. Rosenberg of the NCI. Clinical studies involving IL-2 are being intensively pursued in many hospitals. Advances were reported at our meetings by cancer specialists from the M.D. Anderson Hospital and Tumor Institute at Houston, the Cancer Center at UCLA, the Memorial Sloan-Kettering Cancer Center in New York, and the Dana Farber Cancer Institute at Harvard in Boston.

A National study funded by the NCI began in April at six institutions to duplicate the treatment protocol and confirm the important observations obtained by Dr. Rosenberg and his colleagues. There have been positive responses in patients with renal cell carcinomas, malignant melanomas, and colorectal carcinomas. You will recall that on December 5, 1985, Dr. Rosenberg reported in the *New England Journal of Medicine* the results of treatments of 25 patients using his protocol after standard therapy had failed.

Objective regression of cancer (more than 50 percent of volume) was observed in 11 of the 25 patients: complete tumor regression occurred in 1 patient with metastatic melanoma, and partial responses occurred in 9 patients with pulmonary or hepatic metastases from melanoma, colon cancer, or renal cell cancer and 1 patient with a primary lung adenocarcinoma.

The *New England Journal of Medicine* has recently accepted Dr. Rosenberg's subsequent report concerned with 157 patients. Of these, 108 were treated with a combination of IL-2 and LAK and 49 with IL-2 alone. All these patients were considered terminal with advanced metastatic tumors, after all other types of treatment had failed. Nine of these patients have had complete remission. Seven more are still responding positively. One patient has had remission over 2 years with no recurrence of cancer. This is roughly a 25 percent result or 1 out of 4 patients responding positively to Dr. Rosenberg's treatment. What is more significant about the statistics is that in patients with renal cell cancer over one-half responded positively and of the patients with melanoma, 40 percent responded positively.

When this report is published about 6 weeks from now, it will be more impressive than the original results covered in the December 1985 report. There is no doubt that this protocol is one of the most important tools developed in recent years to combat cancer. There have been some critics who have taken issue with this treatment. However, I think the results speak for themselves. While there have been some toxic effects, in many cases, these can be handled successfully. Some supporters of Dr. Rosenberg have compared his work to the Wright Brothers' airplane at Kitty Hawk. At that time, there was no question of the fact that aviation was in its early stage and held great promise to become the principal means of transportation throughout the world. Dr. Rosenberg's protocol should likewise be considered in its early stages and from it, we are learning a great deal.

Clinical trials of anticancer biologicals have confirmed the effectiveness of both interferon and the new anticancer drug deoxycoformycin (DCF) for the treatment of hairy-cell leukemia, a very rare disease.

Other biological agents are being examined extensively in NCI-supported trials throughout the country. These studies have demonstrated that tumor necrosis factor may be effective for certain cancers. Preclinical studies indicate significant promise against colon and pancreatic cancers.

New research has extensively demonstrated the utility of monoclonal antibodies tagged with radioisotopes for tumor localization in patients with metastatic colon cancer, lymph node tumors, and melanomas. This is the

first step in the scheme for delivery of radiation or drugs or natural toxins directly to targeted tumor tissues, to effect their specific destruction. Monoclonal antibodies have also been used as treatment and produced complete and partial remissions in patients with neuroblastomas, lymphomas, and cancers of the intestinal tract.

A major problem that has confronted oncologists has been the development of resistance to therapeutic agents which initially had inhibited the growth of the patient's tumor. Development of tumor resistance to one drug is often accompanied by concomitant resistance to several other agents to which the tumor had actually never been exposed. This phenomenon of multidrug resistance has obstructed successful drug therapy of cancer. In a major advance last year, researchers identified a drug-binding protein on the surface of multidrug-resistant cells, and the gene that is responsible for production of this protein has now been isolated and cloned. Intensive research is aimed at elucidation of the role of this membrane glycoprotein in the development of multidrug resistance.

Molecular Genetics and Oncogenes

Over the past few years, work supported by the NCI resulted in the discovery that certain genes, called oncogenes, exist within every cell. There are 25 different oncogenes in human cells which may be abnormally amplified or "turned on" as part of the process by which a cell becomes cancerous. Oncogenes, like other cellular genes, direct or control the synthesis of proteins. We now know that the oncogene products are often growth factors or their receptors. Scientists have learned that activation of specific oncogenes can lead to lung cancer, and other specific oncogenes have been identified and isolated from tumors of the kidney, nasal cavity, and peripheral nervous system. Expression of the various oncogenes differs among individual tumors and may provide important information regarding clinical behavior, treatment, and prognosis.

Research in molecular biology supported by the National Cancer Institute continues to underpin the growing biotechnology industry in the United States. Genetic engineering projects resulting from these studies have provided large quantities of purified lymphokines, including IL-2, and have enabled scientists to penetrate the immune system control circuitry. Lymphokines are natural body proteins, present in extremely small amounts, which serve as regulatory signals among the various types of immune cells and are able to amplify the patient's own immunologic assault on the tumor. Research is continuing in this area.

Results which have important clinical implications for surgery and dentistry as well as oncologic medicine have been obtained with transforming growth factor-beta (TGF-beta). This peptide growth factor has been found to play an intrinsic role in inflammation and tissue repair. TGF-beta also stimulates new connective tissue and collagen in animals and can stimulate the formation of new blood vessels.

Recombinant DNA technology and the production of specific monoclonal antibodies have been two powerful adjuncts to new immunologic treatment research. The application of recombinant DNA techniques has also resulted in a number of significant advances in cancer diagnosis. Molecular genetic analyses of osteosarcomas in individuals with inherited retinoblastoma indicate additional alterations in specific chromosomal regions. These studies have led to new potentially curative treatment methods.

New studies suggest that by use of drugs, it may be possible to inhibit oncogene expression or to inactivate its product. With this new knowledge regarding genetic aspects of numerous cancers, chemical methods of tumor control become possible. The National Collaborative Chemoprevention Project has been developed to exploit this new opportunity and to acquire additional basic knowledge in anti-carcinogenesis. Several new biologic agents have been developed this past year and will enter preclinical trials following appropriate tests of efficacy and toxicity.

Molecular genetic studies supported by the National Cancer Institute resulted in discoveries which link the transactivator gene of the HTLV cancer virus with the receptor genes on leukemia cells which are specific for certain lymphokines such as IL-2.

These results have enabled new approaches to genetic reversal methods in those mutant human T cells which produced the leukemias.

Acquired Immune Deficiency Syndrome (AIDS)

Scientists at the NCI discovered the AIDS virus and thus provided medical researchers with a specific target for drug development. NCI has established a formal collaborative effort with the National Institute of Allergy and Infectious Diseases (NIAID) to develop effective therapies for AIDS. The NCI responsibility has been to coordinate and implement preclinical development of new compounds. Preclinical development consists of the identification and/or chemical synthesis of active compounds, laboratory and animal testing of potential anti-AIDS effects, and necessary tests to determine safe starting doses for human studies.

The NCI has also set aside funds to support National Cooperative Drug Discovery Groups. The purpose of this multi-institutional effort is to allow prominent scientists in both industry and academia to collaborate in the development of novel effective therapies for AIDS. This program focuses on encouraging collaboration between prominent scientists that was not possible under standard funding mechanisms. Applications from more than 70 scientific laboratories have been reviewed.

The NCI's Developmental Therapeutics Program, in collaboration with the Food and Drug Administration, has developed an expedited preclinical toxicology process designed to bring promising anti-AIDS drugs to patients as rapidly as possible. This process focuses on generating animal data necessary for the determination of safe starting doses for human testing, minimizes redundancy in data collection, and markedly reduces the time from identification of a promising compound to its entry into clinical trial.

In 1986, less than 2 years after Dr. Samuel Broder and his staff at the NCI found a potentially effective anti-AIDS compound, the NCI intramural clinical program completed a phase I clinical study of azidothymidine (AZT). The study proved the drug could be given safely to patients and demonstrated that some patients had improved immune function during treatment. An extremely significant aspect of AZT therapy is the ability of the drug to cross the blood-brain barrier and arrest the viral destruction of neural tissue. Laboratory tests using AZT in combination with the antiviral acyclovir have resulted in greatly enhanced synergistic action at very low doses *in vitro*. Long-term studies of AZT are continuing, along with widespread effective use of this medicinal throughout the country. The NCI is also studying other anti-AIDS drugs such as suramin, trimetrexate, and other candidate compounds. At present, it is AZT that offers the most exciting promise for successful treatment of AIDS.

It has been discovered that compounds of the 2', 3'-dideoxynucleoside class can effectively inhibit the growth of the AIDS virus in culture. Several compounds, which have similar activity to the original compound, dideoxycytidine, have been synthesized by scientists at the NCI. There is an intensive effort to design drugs with maximum activity against this disease. Dideoxycytidine entered clinical trial in AIDS patients in late 1986. The NCI has developed plans for 1987 drug discovery and development projects which total $17.7 million.

Prevention and Control of Cancer

The NCI is responsible for major programs in cancer prevention and control. These include a broad array of research and application activities related to validation of new methods and evaluation of techniques for screening and detecting cancer in its earliest most treatable stages. The successful program provides physicians and the public with state-of-the-art cancer treatment information. It also provides the Nation with a constant monitoring system for cancer incidence, survival, and mortality.

In 1986, the Community Clinical Oncology Program of the NCI funded 59 community programs in 33 states. Over 1,200 physicians at 200 hospitals participated nationwide. An outreach program was able to incorporate an additional 700 community affiliates, each involving from one to eight physicians, resulting in clinical trial participation on a wide scale in the United States.

Additional National programs include special initiatives for cancer centers, for renovation of and reconstruction of research facilities and for research manpower development. These areas were not sufficiently active in 1986, due to reduced funding priorities in each case. We on the Cancer Panel are particularly concerned about construction and manpower development. If funds are not augmented in these areas, we fear that severe effects of prolonged shortages will be manifest within a very short period of time.

Conclusions

Heretofore, there have been three forms of treatment for cancer; namely, surgery, radiation treatment, and chemotherapy. We now believe there is a fourth approach — biologic therapy and the leader of this is the work of Dr. Steven Rosenberg and his associates. I am pleased to report that excellent progress is being made on all research and control approaches.

National statistics reveal that the incidence of cancer in the U.S., for all sites combined, has increased 5.4 percent over the past 10 years. Over the same time period, the relative survival of treated patients has also increased. The latest figures show 5-year survival rates for whites are 50 percent, and for blacks, 37 percent. When compared to rates in the early to mid-1970s, cancer patients are now living longer, and the survival rates continue to show improvement. For all patients diagnosed and treated in the United States from 1977 through 1982, survival beyond 5 years is currently estimated to be 49 percent.

It is pleasing to report that cancer mortality rates among younger Americans — those under age 55 — have been decreasing. Decreases in mortality are now observed for all sites combined, despite increasing incidence in this age group. There is a decline in colon and rectal cancer mortality at all ages in the U.S., also in the face of increasing incidence. These data indicate that treatment is increasingly effective, or there is better patient management, or that patients are being detected at earlier, more treatable stages, or all three may be true.

The evidence against smoking continues to grow. A study of lung cancer among nonsmoking women suggests an increased risk in proportion to the number of cigarettes their husbands smoke. For many years the National Cancer Advisory Board has taken strong stands against the use of tobacco. Smoking alone is estimated to cause 30 percent of all cancer deaths each year, and this year the Board was delighted to hear that lung cancer incidence in white men has begun to decline, following the decline in smoking prevalence among these men. It proves that quitting smoking can

prevent cancer. I strongly support any mechanism that assists getting this message to the American people.

I believe that Dr. Vincent DeVita, Jr., the Director of NCI, is doing outstanding work. His medical expertise is matched by his superb managerial qualities.

Fifteen years ago President Nixon signed the National Cancer Act into law, initiating a period of growth and unprecedented discovery in basic research in all of biology and medicine. The National Cancer Institute itself is marking its 50th anniversary in 1987, and the National Institutes of Health is celebrating its 100th birthday. However, science and medicine in the most recent few years have produced more and greater discoveries of benefit to mankind than were possible in the previous century. This has come about due to the foresight of the Federal administrations 15 and 50 years ago, when Congress and the President clearly enunciated that investments in basic biomedical research were invaluable guarantees for future advances and developments. For the continued strength and success of the Nation, it is imperative that we keep up this drive.

This report has been prepared with the cooperation and approval of my colleagues, Dr. William P. Longmire, Jr. and Dr. John A. Montgomery.

Armand Hammer

Dr. Armand Hammer, Chairman
The President's Cancer Panel

Concurred:

William P. Longmire Jr

Dr. William P. Longmire, Jr.

John A. Montgomery

Dr. John A. Montgomery

President's Cancer Panel

National Cancer Program National Cancer Institute

March 31, 1987

The Honorable George Bush
President of the Senate
Washington, DC 20510

Dear Mr. President:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report I recently submitted to President Reagan. Section 415(b) of the Health Research Extension Act of 1985 requires that the report to the President also be made available to the President of the Senate and the Speaker of the House.

Copies are also being made available to various members of the Senate and House with special interest in health-related matters.

As noted in my transmittal letter to the President, the goal we pursue is tremendously important — the removal of cancer from its preeminent position as the most dreaded of diseases afflicting mankind. We cannot achieve that goal without continued and increased Federal support for the National Cancer Institute. I hope we can count on you for such support in the year ahead.

With very best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

President's Cancer Panel

National Cancer Program National Cancer Institute

April 6, 1987

The Honorable Robert C. Byrd
Majority Leader
United States Senate
S-221 Capitol Building
Washington, DC 20510

Dear Senator Byrd:

As Chairman of the President's Cancer Panel, I am required to report periodically to the President on the status of the National Cancer Program as operated by the National Cancer Institute. Because of your important position in the Senate, I thought you would be interested in my most recent report, a copy of which is attached.

As I noted in my transmittal letter to the President, the goal we pursue is tremendously important — the removal of cancer from its preeminent position as the most dreaded of diseases afflicting mankind. We cannot achieve that goal without continued and increased Federal support for the National Cancer Institute. I hope we can count on you for such support in the year ahead.

With best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

President's Cancer Panel

National Cancer Program National Cancer Institute

March 31, 1987

The Honorable Jim Wright
Speaker of the House of Representatives
Capitol Building, H-204
Washington, DC 20515

Dear Mr. Speaker:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report I recently submitted to President Reagan. Section 415(b) of the Health Research Extension Act of 1985 requires that the report to the President also be made available to the President of the Senate and the Speaker of the House.

Copies are also being made available to various members of the Senate and House with special interest in health-related matters.

As I noted in my transmittal letter to the President, the goal we pursue is tremendously important — the removal of cancer from its preeminent position as the most dreaded of diseases afflicting mankind. We cannot achieve that goal without continued and increased Federal support for the National Cancer Institute, which is doing an excellent job. I hope we can count on you for such support in the year ahead.

With very best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

President's Cancer Panel

National Cancer Program National Cancer Institute

March 31, 1987

The Honorable Otis R. Bowen
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Mr. Secretary:

I am pleased to enclose a copy of the report I have recently submitted to the President on the status of the National Cancer Program, as operated by the National Cancer Institute. Copies have also been made available to the President of the Senate and the Speaker of the House, as required by law, as well as to other members of the Congress.

You will be especially interested, I believe, in the description of the work at the National Cancer Institute involving lymphokine-activated killer cells and Interleukin-2, under the leadership of Dr. Steven Rosenberg. This is one of the most important developments in cancer research and treatment in the past decade.

My colleagues and I believe the NCI is extremely well managed by its distinguished Director, Dr. Vincent DeVita. While much remains to be done, we are convinced we are gaining steadily in the fight against cancer, largely due to the Federal support provided to the NCI and through it to the cancer community at large. We hope such support will be continued and strengthened in the years ahead.

With best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

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