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Attachment J

Report of the Chairman to the President,

January 1 to December 31, 1986

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

National Cancer Institute

NIH Publication
No. 87-2609
April 1987

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President's Cancer Panel

National Cancer Program National Cancer Institute

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 Thera-

peutics 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.

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

Concurred:

Dr. William P. Longmire, Jr.

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

Executive Secretary:
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20205
Phone: 301-496-1148

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

Executive Secretary
Dr Elliott H Stonehill
National Cancer Institute
Bethesda, MD 20205
Phone 301-496-1148

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

Attachment K

Report of the Chairman to the President,

January 1 to December 31, 1987

January 1 to December 31, 1987

President's Cancer Panel

Report of the Chairman

U.S. Department of Health and Human Services

Public Health Service

National Institutes of Health

National Cancer Institute

NIH Publication
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PANEL MEMBERS

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Birmingham, AL 35255

President's Cancer Panel

National Cancer Program National Cancer Institute

February 25, 1988

The President
The White House
Washington, D.C. 20500

Dear Mr. President:

Section 415 (b) of the Health Research Extension Act of 1985 requires that, as Chairman of your President's Cancer Panel, I report to you annually on the National Cancer Program as operated by the National Cancer Institute. My report for 1987 is attached hereto.

The report is a positive one, and I am pleased to note that under your Administration real progress is being made in the fight against cancer. My colleagues on the Panel, Dr. John Montgomery and Dr. William Longmire, agree with me that as a result of the efforts of the National Cancer Institute cancer patients are benefitting in an unprecedented manner from research in basic cancer biology and the swift clinical translation of the most important advances.

Some of the highlights of my report cover advances in the field of biological response modifiers, particularly use of interleukin-2 and a relatively new discovery of certain hormones which involve production of white blood cells in the bone marrow, called the colony stimulating factors (CSFs).

I have reported to you previously on the remarkable work being done at the National Cancer Institute by Dr. Steven Rosenberg using interleukin-2 and lymphokine-activated killer cells (LAKs). This work has been expanded to six national cancer centers and the results have confirmed the effectiveness of this treatment in advanced cancer cases. Further expansion is being planned for this protocol.

Dr. Rosenberg has now developed a very exciting new treatment which uses interleukin-2 and tumor infiltrating lymphocytes (TILs). These are lymphocytes which are taken from a patient's own tumor and combined with interleukin-2 and the cancer drug cytoxan. This treatment has produced dramatic results in the first seven patients treated by Dr. Rosenberg. Two patients achieved complete regression of their tumors and four out of the other five had more than 50 percent reduction in the size of their tumors. I have every confidence that Dr. Rosenberg will continue to have excellent results with this new protocol.

One of the year's most important advances is the use of the colony stimulating factors. One of the CSFs, the factor called G-CSF, has been used in the treatment of advanced bladder cancer patients at Memorial Sloan-Kettering Cancer Center in New York. Used in combination with a drug treatment called M-VAC, the G-CSF was shown to have restored many of the immune cells of the patients to their original state after chemotherapy. As you know, we are limited in our use of chemotherapy because it so often destroys the cells of the immune system while destroying the cancer cells. However, the G-CSF brought those cells back into an effective state. This is a very encouraging development, and I believe that by reducing so effectively the toxic effects of chemotherapy, we will dramatically improve the survival of cancer patients.

Finally, I would call your attention to my suggestion that the Government provide matching funds to private funds which we will endeavor to raise over the next two years, up to $500 million. This is to be a bipartisan effort in the Congress, and I have already spoken to Jim Wright, Tony Coelho, Ted Stevens and Alan Simpson on the matter. We will endeavor to interest other members of both Parties. It is my firm belief that with sufficient funds we can conquer cancer just as we have conquered polio, diphtheria, small pox, tuberculosis and scarlet fever. I am willing to undertake a campaign for this purpose, and I feel we can succeed in this undertaking. Whatever we develop in cancer research may prove to be valuable in combatting AIDS, which also involves failure of the immune system.

Mr. President, it is a great privilege to serve as Chairman of your Cancer Panel. It is my hope, and that of my colleagues, that this report will prove useful to you and others in the Administration. I am always ready to assist you in any way possible as you carry out your tremendous responsibilities in leading the country towards peace and prosperity for all.

With warmest regards,

Respectfully,

AH:ec

Attachment

1987 CHAIRMAN'S REPORT TO THE PRESIDENT

During 1987 important discoveries in cancer research were made, and the President's Cancer Panel observed significant advances in treatments for cancer in the United States. The use of biologics in treatment has made remarkable strides; molecular genetics has advanced further into causation and control; research progress in drug development, virology and cell biology has advanced our ability to attack this dread disease, and additional national programs have been initiated to enhance cancer prevention and control.

Dr. William P. Longmire, Jr., and Dr. John A. Montgomery, my colleagues on the President's Cancer Panel, and Dr. Vincent T. DeVita, Jr., Director of the National Cancer Institute (NCI), accompanied me as I convened meetings of the Panel in Los Angeles, Pittsburgh, and Bethesda during 1987. We heard testimony regarding innovations in cancer treatments for skin cancer (melanoma), lung cancer, breast, colon and rectal cancers, and learned of discoveries relating to the role played by a cascade of genes (oncogenes) in these diseases.

The members of your Cancer Panel also attended the meetings of the National Cancer Advisory Board, where we reviewed the status of the National Cancer Program in all its aspects.

This report concerns the current status of the National Cancer Program as monitored by the President's Cancer Panel and describes some of the significant achievements of the year.

Cancer Treatment

The biologic attack on cancer continues to be vigorously pursued by the NCI, as I reported in 1985. As you know, at that time I related the exciting work of Dr. Steven Rosenberg using the adoptive immunotherapy procedure with LAK (lymphokine-activated "killer cells") and interleukin-2 (a naturally occurring substance called a "biological response modifier"), as well as work being done with monoclonal antibodies and another biological response modifier called TNF (tumor necrosis factor). There have been impressive new gains in these areas this year.

Approval was obtained from the Food and Drug Administration (FDA) in April to expand the clinical trials of two experimental therapies to a national level.

One program is the interleukin-2 (IL-2) plus the lymphokine-activated killer cells (LAK), and the other therapy is using IL-2 alone. Since FDA approval, over 100 patients have been treated at the following six cancer centers:

City of Hope, Los Angeles, California
Veterans Hospital, San Antonio, Texas
Loyola Medical Center, Chicago, Illinois
Montefiore Medical Center, New York, New York
University of California San Francisco Medical School, San Francisco, California
New England Medical Center, Boston, Massachusetts

Up to 30 percent of these patients, with advanced skin cancers and advanced kidney cancer, unresponsive to previously known therapies, have responded to the new treatments. At present, these national clinical trials have produced complete disappearance of cancer in 11 percent of the kidney cancer cases and 6 percent of the skin cancers, or melanomas. For this latter small group of patients, this response is the difference between normal life and death.

New trials will begin shortly at additional centers to pursue a new and even more effective treatment protocol with IL-2. Dr. Steven Rosenberg has discovered an enrichment technique to isolate, from the patient's tumor, white blood cells called tumor infiltrating lymphocytes (TIL) which, when reinjected into the patient with IL-2, has resulted in excellent responses in all of the last four patients treated. Initially this treatment was shown to cure leukemic mice.

Also this year, a highly effective drug therapy regimen for advanced bladder cancer has been effected by Dr. Allan Yagoda at Memorial Sloan-Kettering where 92 terminal patients have been treated. This common tumor has heretofore been unresponsive to treatment when it extends beyond the surface of the bladder. The treatment, called M-VAC, uses four drugs: methotrexate, vinblastine, adriamycin, and cis-platinum. About 40 percent of the patients have achieved complete remissions. A high priority national clinical trial has been established to test M-VAC use in conjunction with surgery in order to reduce mortality.

Unfortunately, lung cancer mortality continues to obscure signs of progress. It is responsible for 135,000, or 30 percent of all cancer deaths annually. Because it is so common and refractory to therapy, the NCI organized special lung cancer study groups over 10 years ago to examine the pathology, diagnosis, immunology, genetics, and treatment of lung cancers. Clinical trials were undertaken, and this year the results show that even in this devastating disease, those patients who had surgery followed by radiation and chemotherapy, showed a significant improvement in disease-free survival. However, 25 percent of the group not receiving drug therapy achieved the same overall survival rate. Smoking is the dominant cause of lung cancer today, despite the warnings in ads and the Surgeon General's efforts which have undoubtedly helped control the spread of smoking. The need for further intensive research on the disease is obvious.

A major problem today is the development of more effective treatment for patients with advanced, drug-resistant cancers. For example, while the majority of patients with ovarian, breast, head and neck, and small cell lung cancer respond to initial drug therapy, many relapse with drug-

resistant tumors. Other malignancies are poorly responsive to available chemotherapy.

During the past year, the tools of molecular biology and recombinant DNA technology (a genetic engineering means by which genes can be changed and duplicated) have taught us much about the underlying mechanisms of tumor cell resistance to drugs. A family of genes responsible for multidrug resistance of human tumor cells has been isolated. These genes code for a membrane protein called P170, which is believed to be a pump that moves toxic chemicals out of cells. Cancer cells appear to have adapted this pump to avoid the lethal effects of cancer drugs. The amount of P170 in drug-resistant cancer cell membranes is much greater than the amount in normal body cells.

The evolving understanding of drug resistance is having a major impact on strategies used to identify new anticancer drugs for clinical trials. This has led to drug-screening techniques using drug-resistant human cells, with high levels of P170, to select drugs that work in its presence.

In the past two years, the NCI Drug Development Program has undertaken fundamental new directions in terms of both the sources of new compounds and the test systems used to detect active drugs, redesigning the screening system to utilize human cancer cells grown in the laboratory as an alternative to mouse cancers. The Institute believes that these systems, not available a decade ago, have great promise in predicting drug effects on human tumors more accurately. The capacity of the new drug screening system will increase to enable testing of over 10,000 new compounds per year when it is fully implemented in February of 1988. The NCI has established this new screen at no new cost by phasing it in as the old system is eliminated.

Ipomeanol, a product of sweet potato mold, is an example of a highly specific drug currently under development. It has been identified as selectively active against human bronchoalveolar carcinoma, a human lung cancer, in experimental animals; under treatment these normally fatal malignancies regress entirely. An application to initiate clinical trials of ipomeanol was filed with the FDA in November of 1987.

Molecular Genetics: The Biologic Revolution and Control of Gene Regulation

At present we know that the regulation of gene expression, or the selective "turning on" and "turning off" of genes in a cell, is largely a response of the cell to its microenvironment. Most cancers are believed to occur when the control of genes that regulate cell growth breaks down; therefore, understanding the biological and chemical rules of gene regulation and modification is critical to treating, preventing, and controlling cancer. Because of its importance in the initiation and progression of cancer, researchers are studying the process of gene regulation at the most fundamental levels of DNA structure, that is deoxyribonucleic acid, the molecular basis of heredity in organisms. NCI researchers have utilized recombinant DNA techniques to construct artificial genes containing the necessary control signals to convert cancer cells to normal cells. Intensive efforts are directed toward methods to successfully integrate these genes into the appropriate cancer cells derived from patients.

With new knowledge of gene regulation, it is now possible to understand why some tumor viruses can cause cancerous development of certain cell types, and why cancers often result from chromosomal rearrangements. More than 90 percent of human malignancies involve some form of cytogenetic change, and research is currently focused on understanding these changes.

An example of understanding how gene regulation controls the cancer process is the new use of transgenic mouse models. Cloned foreign genes (nonmouse) are introduced into the germ lines of these animals, which then acquire the characteristics of the foreign genes. These transgenic mice are used to study human diseases induced by these genes, including AIDS. The success of transgenic mouse studies has implications for use in therapy that focuses on turning genes off and on in cells to prevent and treat certain forms of cancer.

Research supported by the NCI has recently uncovered another important component of the oncogene cascade, antioncogenes or suppressor genes, whose loss from cells appears to cause cancerous growth. Inheritable tumors such as retinoblastoma and Wilms' tumor have provided the first clear evidence of the existence of antioncogenes. Wilms' tumor cells return to their normal functioning when the missing suppressor gene is reinserted, using somatic cell hybridization genetics. The cloning of the retinoblastoma gene is a major breakthrough as it permits the study of all the structural and regulatory elements of an antioncogene. Recently this extraordinary advance was multiplied in importance by the discovery of similar recessive genes in common cancers like breast and lung cancer.

Biological Response Modifiers

Biological response modifiers (BRMs) offer some of the most exciting applications of recombinant DNA technology. BRMs are substances normally made by cells of the immune system in response to a foreign body or an infection. Examples of BRMs are antibodies, interleukins (discussed under Cancer Treatment above), and interferons and colony stimulating factors (CSFs). Using recombinant DNA technology, highly purified preparations of these, and other BRMs, are now being made in sufficient quantities for use in clinical trials.

One of the year's most important advances in biologics is the use of colony stimulating factors. CSFs are hormones involved in the production of blood elements in the bone marrow. Similar to growth factors that stimulate cancer cells to proliferate, CSFs regulate the division of normal bone marrow elements. CSFs protect animals from the side effects of drug and radiation treatments. This research has resulted in using CSFs to obtain effective cancer

treatment with reduced side effects and has been incorporated into the protocol with the M-VAC therapy for bladder cancer described above.

This year interferon was approved by the FDA for the treatment of hairy cell leukemia. It is also effective in chronic myelocytic leukemia and has promise for malignant melanoma and kidney cancer. Clinical trials are now under way with interferons in combination with tumor necrosis factor, with monoclonal antibodies, and with other therapeutic agents.

Acquired Immune Deficiency Syndrome (AIDS)

The continued spread of the AIDS epidemic warrants new and extensive epidemiologic studies to define risk factors important to the spread of the infection. The potential spread of AIDS to the heterosexual population, the increasing incidence of AIDS among women and children, the increase of AIDS-associated malignancies, and the possibility of other viruses acting as cofactors in determining the severity of the AIDS infection or the incidence of malignancies in AIDS patients, are all areas that need additional study.

The NCI has been a leader in the AIDS research effort since the recognition of the disease in 1981. Previous NCI work on cancer viruses permitted the rapid discovery of HIV, the virus which causes AIDS. The NCI experience in drug development led to the rapid recognition in this program of azidothymidine (AZT), a drug first synthesized in 1964, as a potential anti-AIDS drug.

AZT is effective in prolonging the lives of some AIDS patients and is now available by prescription for the majority of patients. It reduces the occurrence of life-threatening opportunistic infections and has been effective in treating the dementia frequently seen in AIDS patients.

Other agents are under study, including dideoxycytidine (DDC), which is in an early phase of patient testing. In cell culture, this compound is more potent against the AIDS virus than AZT. A pilot study combining AZT and DDC has been initiated by NCI.

Without the enzyme "reverse transcriptase," the AIDS virus cannot multiply. Scientists at the NCI's Frederick Cancer Research Facility have now cloned the reverse transcriptase gene of HIV. This important event has two immediately significant implications for AIDS drug development. First, the availability of large amounts of pure enzyme will enable a directed attack on the virus' reproductive machinery, and second, research efforts can now be directed toward rationally designed drugs that interact specifically with the target enzyme.

The recently discovered laboratory procedure that amplifies the HIV DNA up to 1,000,000 times provides an extremely sensitive and specific test for the virus and may permit its detection at levels far below those of currently utilized procedures. Its use may permit therapeutic intervention at much earlier stages of infection.

This year scientists have also developed a new drug treatment for Pneumocystis carinii pneumonia (PCP) in AIDS patients. PCP is the most commonly recognized life-threatening infection in AIDS patients. It occurs in 80 percent of patients and is responsible for over one-third of all deaths. The new treatment uses the anticancer drug trimetrexate in combination with its antidote, leucovorin, which protects the patient from the toxic effects of the drug. Trimetrexate proved to be a safe and effective therapy for PCP in a study conducted by scientists at the NCI.

A new human B-cell virus, HBLV, has been isolated recently from AIDS lymphoma patients. It is immunologically and genetically distinct from other known human leukemia viruses. Researchers are actively studying the distribution of this new virus, and its relationship to lymphomas in non-AIDS patients.

Prevention and Control of Cancer

I believe the current goal of 50 percent reduction in cancer deaths by the year 2000 is not enough. This would mean millions of people would die before then and thereafter. In view of the progress cancer research has made in enhancing the body's own immune system to fight cancer, I feel such a goal is too low, and we should set our sights much higher. So much progress has been made in the past few years that the means to achieve a much higher goal may be available, if we can only take advantage of them in an effective way.

Much of the improvement in survival in the past decade can be traced to widespread participation of cancer patients in clinical trials. Increased minority participation in clinical trials will lead to improved minority cure and survival rates. The Panel feels this effort must be rapidly and effectively implemented, with adequate financial support.

The following are some of the parameters that cancer researchers consider in their work:

- Smoking is directly responsible for 30 percent of all cancer deaths.
- Diet and nutrition may be related to 35 percent or more, of cancer deaths.
- Screening for breast and cervical cancer are effective in reducing mortality.
- Widespread application of state-of-the-art cancer treatment could reduce mortality rates.
- Gains in treatment are continuing unabated.

Since the passage of the National Cancer Act, the NCI has developed and supported an extensive national network to implement the National Cancer Program to achieve these goals. The network was completed in 1984. The major components include:

- Sixty designated cancer centers that serve as the regional foci for research, clinical studies, education, and cancer control. The centers support major research efforts of the nation's clinical and academic scientists.
- The Community Clinical Oncology Program (CCOP) maintains 50 programs across the country to conduct national clinical trials involving community physicians.

- The Clinical Cooperative Groups (CCG) that consist of 18 multi-institutional consortia of 5,000 clinical investigators, who conduct a variety of new cancer clinical trials with over 25,000 patients annually.
- The Cooperative Group Outreach (CGO) Program designed to upgrade the skills of community physicians and other health professionals by advanced training.
- The Surveillance, Epidemiology, and End Results (SEER) Program, which tracks cancer incidence, mortality and survival, and provides measures of overall program progress and direction for future prevention and control efforts.
- The Cancer Information System (CIS), which is a national toll-free telephone service, providing immediate answers to cancer-related questions from cancer patients, their families, the general public, and health professionals.
- Physician Data Query (PDQ), which is an online information system about cancer treatment and cancer research protocols for community-based doctors. It is accessible by computer through the National Library of Medicine, private information system vendors, and the Cancer Information System.

The Panel recognizes that although this basic network of resources is in place, an expansion is imperative to achieve our goals.

The members of the Panel encourage this increased support for national centers and clinical trials, while maintaining the support for basic research that led to the advances described above. By setting ambitious but achievable objectives and by promoting actions that can have an effect on cancer incidence and mortality, the NCI has set the standard for the nation in public health measures to control the disease that still kills one American almost every minute.

Conclusions

This year the NCI marked its 50th anniversary as an Institute of the National Institutes of Health, and also its 15th year since passage of the National Cancer Act. As Chairman of the President's Cancer Panel for the past six years, I have intensively studied the National Cancer Program as it is being promulgated from Bethesda, and as it is being received and implemented across the nation. My colleagues and I agree that as a result of the efforts of the National Cancer Institute cancer patients are benefitting in an unprecedented manner from research in basic cancer biology and the swift clinical translation of the most important advances. We agree that the biologic revolution fostered by the National Cancer Act has made the current progress possible.

The sophisticated techniques of molecular genetics have provided an understanding of gene regulation that has revolutionized the field of tumor biology. We now possess insight into the changes in the genetic makeup of cells that lead to malignancy.

Recombinant DNA technology has led to the development of new biological therapies on a scale that will make them available to a wide patient population, therapies such as monoclonal antibodies, colony stimulating factors, the interleukins, and others. Clinical successes with these biologicals continue to grow. Recombinant DNA technology also has paid dividends in the areas of cancer detection and diagnosis. On the economic level, the biological revolution has provided the foundation for the robust multibillion dollar biotechnology industry in the United States.

The nation's investment in cancer research continues to pay off in the clinical area, where combined modality treatments have improved survival for thousands of cancer patients. The NCI continues its excellent program for drug discovery and development, seeking new and improved agents for cancer therapy.

The NCI's network of programs for technology transfer mandated by the Cancer Act has produced extensive benefits in basic research, and in cancer prevention, control, and treatment. As the Institute continues to modify and strengthen the components of this network, the capacity to respond rapidly and effectively to new initiatives, to reduce cancer incidence, morbidity, and mortality, will grow, and the dividends to the American public can only increase.

We know that cancer can be controlled. Eliminating cancer requires continued vigorous basic research to understand fully the causes and to develop cures for all its multiple forms. Thus, I suggest that the Government provide matching funds to private funds which we will endeavor to raise over the next few years up to $500 million. This would be a bipartisan effort in the Congress. We should enlist all private groups and organizations in this effort which touches us all, directly or indirectly. Let us make our long-range goal the elimination of all cancers and not be satisfied with 50 percent reduction in cancer deaths by the year 2000. Cancer, after all, is a disease. Just as we conquered polio, diphtheria, small pox, tuberculosis, and scarlet fever, we can conquer cancer if we have the funds.

Armand Hammer
Chairman
President Cancer Panel
Feb 25, 1988

President's Cancer Panel

National Cancer Program National Cancer Institute

Executive Secretary
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20892
Phone: 301-496-1148

February 29, 1988

The Honorable George Bush
President of the Senate
The Capitol 212
Washington, DC 20510

Dear Mr. President:

As Chairman of the President's Cancer Panel, I have compiled the attached report to the President pursuant to Section 415 (b) of the Health Research Extension Act of 1985. This section also requires that the report be made available to the President of the Senate, and a copy is enclosed accordingly.

Copies of the report are also being sent to various members of the Congress with special interest in health-related matters.

As I noted in the letter to the President, the report is a positive one. I would like to call your attention to my suggestion that the Government provide matching funds to private funds which we will endeavor to raise over the next two years. The private effort would endeavor to raise $500 million, which we hope the Government would match. These funds would be separate from the National Cancer Institute budget as approved by the Congress each year. The private effort will be launched at a luncheon in New York March 1st. The projects to be supported by the additional funds are covered in the so-called By-Pass Budget prepared by the National Cancer Institute, a copy of which I enclose. I call your attention to page 5 of the budget for the specific projects to which such funds would be applied.

This is a very important effort involving the private sector and the Government in a cause that is vital to all Americans. I hope you will find this project worthy of your support.

With very best wishes,

Sincerely,

Armand Hammer

Chairman

Attachments

President's Cancer Panel

National Cancer Program National Cancer Institute

Executive Secretary
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20892
Phone: 301-496-1148

February 29, 1988

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 have prepared the attached report to the President on the status of the National Cancer Program as operated by the National Cancer Institute. Because of the vital role you play in the Senate in health-related matters, I thought you would find the report of interest.

As noted in my transmittal letter to the President, the report is a positive one and progress against this dread disease is being made. To my mind, however, the progress is not fast enough, and I would like to call your attention to a suggestion I have made in the report that the Government provide matching funds to private funds which we will endeavor to raise over the next two years. The private effort would attempt to raise $500 million which we hope the Government would then match.

These funds would be separate from the National Cancer Institute budget as approved by the Congress each year. These funds would be used for many worthwhile projects which cannot be funded at present. For example, only 36 percent of approved research projects are being funded at present. We would like to raise this figure much higher. Also, we need to increase the number of clinical trials in the field of biologicals, put increased emphasis on technology transfer, and increase prevention activities by 65 percent.

A budget has been prepared by the NCI under the provisions of the National Cancer Act, which is known as the By-Pass Budget. The projects to be supported by the additional funds raised by private efforts and matched by the Government would be taken in large part from the recommendations of this budget, because full scientific justification exists for all these projects with the approval of the National Cancer Advisory Board, as well as the President's Cancer Panel and the Boards of Scientific Counselors of the NCI.

I enclose a copy of this budget for your information and call your attention to page 5 for specific projects to be funded.

The project which I am proposing is called "Stop Cancer" and will be launched at a luncheon in New York on Tuesday, March 1st. Approximately 475,000 people died last year from cancer, and this disease will strike one out of every four Americans. These figures are unacceptable. This project offers a real opportunity for private enterprise and the Government to work together in a cause which is of the utmost importance to all Americans. I hope we can count on your support for this effort.

With best wishes,

Sincerely,

Chairman

Attachments
1-report
2-budget

President's Cancer Panel

National Cancer Program National Cancer Institute

Executive Secretary:
Dr. Elliott H. Stonenill
National Cancer Institute
Bethesda, MD 20892
Phone: 301-496-1148

February 29, 1988

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

Dear Mr. Secretary:

It was a great pleasure to meet you last Thursday in the Oval Office meeting with President Reagan.

As required by the Health Research Extension Act of 1985 (Section 415 b), I am formally submitting a copy of my report to the President to you in your capacity as Secretary of Health and Human Services.

I have also sent copies of the report to the President of the Senate and the Speaker of the House and to various members of the Congress with special interest in health-related matters.

As noted in my cover letter to the President, the report is a positive one. Under the Reagan administration much progress has been made in cancer research and treatment. However, much more could be done and it is for this purpose that I have made the recommendation that the Government provide matching funds to private funds which we will endeavor to raise over the next two years. The private effort would endeavor to raise $500 million, which we hope the Government would match. These funds would be separate from the NCI budget as approved by the Congress each year. This private effort will be launched at a luncheon in New York March 1st. I will keep you informed as this project develops.

This is a very important effort involving the private sector and the Government in a cause that is vital to all Americans. I hope you will find this project worthy of your support.

With best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

President's Cancer Panel

National Cancer Program National Cancer Institute

Executive Secretary
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20892
Phone: 301-496-1148

February 29, 1988

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 have prepared the attached report to the President pursuant to Section 415 (b) of the Health Research Extension Act of 1985. This law also requires that the report be made available to the President of the Senate and the Speaker of the House, and a copy is enclosed accordingly.

Copies are also being sent to various members of the Congress with special interest in health-related matters.

As noted in my cover letter to the President, the report is a positive one. I have already spoken to you concerning my suggestion that the Government provide matching funds to private funds which we will endeavor to raise over the next two years. The private effort would endeavor to raise $500 million, which we hope the Government would match. These funds would be separate from the National Cancer Institute budget as approved by the Congress each year. The private effort will be launched at a luncheon in New York March 1st. Congressman Tony Coelho will be present, and I am sure he will report to you on the effort. The projects to be supported by the additional funds are covered in the so-called By-Pass Budget prepared by the National Cancer Institute, a copy of which I enclose. I call your attention to page 5 of the budget for the specific projects to which such funds would be applied.

I very much appreciate your cooperation in this matter and know that with your support we will have a much better chance of success.

With very best wishes,

Sincerely,

Armand Hammer

Chairman

Attachments
Report
By-Pass Budget

Attachment L

Report of the Chairman to the President,

January 1 to December 31, 1988

January 1 to December 31, 1988

President's Cancer Panel

Report of the Chairman

U.S. Department of Health and Human Services

Public Health Service

National Institutes of Health

National Cancer Institute

NIH Publication
No. 89-2609
November 1989

President's Cancer Panel

National Cancer Program National Cancer Institute

November 1, 1989

The Honorable George Bush
The President
The White House
Washington, DC 20500

Dear Mr. President:

As mandated by the Health Omnibus Extension Act of 1988, I am pleased to submit, as Chairman of the President's Cancer Panel, my report on the National Cancer Program for 1988.

My colleagues on the Panel, Dr. William P. Longmire and Dr. John A. Montgomery, agree with me that the National Cancer Program as operated by the National Cancer Institute is extremely well managed and has produced tangible benefits for cancer victims throughout the country. We feel the continued progress in research and the advances in treatment obtained in the past year have come about as a result of a well-balanced program and the effective use of funding.

Some of the highlights of my report cover a successful new treatment that overcomes previous resistance to chemotherapeutic drugs; development of immunotoxins to seek and destroy target cells in cancer patients; a significant advance in adjuvant therapy for breast cancer patients utilizing hormone therapy or chemotherapy following surgery; the discovery of a new group of genes that suppress the development of cancer cells; and the development of promising approaches to the prevention of cancer.

But perhaps the most promising development involves the work of Dr. Steven A. Rosenberg, Chief of the Surgical Branch of the National Cancer Institute. Dr. Rosenberg has developed the technique of adoptive immunotherapy in which the body's own defense mechanism — the immune system — is utilized to kill cancer cells. White blood cells, called lymphocytes, taken from the patients are treated with the biological growth factor known as interleukin-2 (IL-2) and converted into lymphokine-activated killer cells (LAK cells). These LAK cells, when injected back into the patients, can kill cancer cells. Patients with advanced melanoma and renal cancer, who did not respond to any other known therapy, have been treated effectively with this technique, which is now available at some 39 cancer centers throughout the country.

Dr. Rosenberg and his colleagues have continued their research with adoptive immunotherapy and this year made an extraordinary advance by isolating and culturing tumor-infiltrating lymphocytes (TILs) from patients' own tumors. TIL cells are grown with IL-2 in laboratory cultures and then are reinjected into the patients. In laboratory tests this therapy appeared almost 100 times more effective in destroying cancer cells than the LAK/IL-2 protocol. In addition the TIL/IL-2 procedures incorporated the anticancer drug cyclophosphamide. The initial study, as reported in the December 22, 1988, issue of the *New England Journal of Medicine,* resulted in at least a 50-percent reduction of tumors in 60 percent of patients with malignant melanoma which had metastasized to other parts of the body. This remarkable response rate is the highest ever reported for treatment of advanced melanomas. The development of LAK cells, TILs, colony-stimulating factors, and other biological response modifiers has now added a fourth form of cancer therapy to the traditional three previously in existence; surgery, chemotherapy, and radiation. This new biological therapy will have a dramatic effect in reducing cancer fatalities in the future in my opinion.

Dr. Rosenberg and his colleagues have just recently taken an additional significant step in immunotherapy. They have inserted an altered gene into the TILs and transferred this gene into patients suffering from advanced cancers. It will take several months to complete all the tests and evaluations on the patients so treated, but the results to date have been very encouraging, and it is clear this is a major advancement that would be of great benefit to cancer victims in the future. Dr. Rosenberg has told me that work such as his could not have been undertaken so successfully at any institution other than the National Cancer Institute.

I would also like you to note that the two recipients of the 1989 Nobel Prize for Medicine, Dr. Michael Bishop and Dr. Harold Varmus, have been supported in their work for many years by grants from the National Cancer Institute. As you are aware, their pioneering work in the discovery of cancer-causing genes present in the body (known as oncogenes) is one of the most significant developments in cancer research in the last few decades, and offers great promise for discovering the basic causes of cancer. Both Dr. Bishop and Dr. Varmus received their early training at the National Cancer Institute, which is a tribute to the caliber of research and training provided at the NCI. In addition, Dr. Bishop and Dr. Varmus were two of the first recipients of the grants known as the Outstanding Investigator Grants, a mechanism developed by your Cancer Panel to stimulate research by investigators with a proven record of accomplishment in cancer research. I was personally very pleased by the selection of these two outstanding scientists as recipients of the Nobel Prize for Medicine since I was able to recognize the caliber of their work in 1982 when I gave them one of the very first Hammer Cancer Prize awards.

However, while we have made major achievements in cancer therapy, hundreds of thousands of people die each year from cancer. Furthermore, despite rapid progress in cancer research and more effective efforts at prevention, cancer — largely because of the aging of the American population — will soon become the number one killer in the United States. We cannot be complacent about this dreadful probability.

The Panel is very concerned that recent budget increases for cancer research and training have not been sufficient even to sustain existing activities. Only 25 percent of approved grants will be funded by the National Cancer Institute this year due to budget restraints. This means that 75 percent of very good research is not being pursued, research that could possibly lead to the final solution of the cancer problem.

I recognize, of course, that this is a time when government spending must be restrained, but we are in danger of losing the momentum that has been built up with so much effort over the past several years.

In an effort to prevent this from happening, I have established the STOP CANCER campaign, of which you are aware. I want to put all of our best scientific minds to work on finding a cure for cancer, not just a small percent of them. As you know, I hope to raise $500 million in private funds over the next 4 years for the National Cancer Institute. The campaign is going well, and we have to date raised $12.5 million with only one major fundraising event.

Mr. President, it is a great privilege to serve as Chairman of your Cancer Panel. I hope this report will prove useful to you and others in your Administration. I wish you great success in the awesome responsibility you have assumed and have every confidence in your ability to lead this great country toward a future of peace and prosperity for all.

With warmest regards,

Respectfully,

Chairman

Attachment

cc: Dr. William P. Longmire
Dr. John A. Montgomery

1988 CHAIRMAN'S REPORT TO THE PRESIDENT

In 1988 the President's Cancer Panel witnessed significant and remarkable progress in cancer research in this country. These advances were made in the laboratories and hospital rooms of the National Cancer Institute (NCI) in Bethesda, and also in hospitals and laboratories nationwide, in research programs supported by the NCI.

Maintaining the successful approach initiated in 1981, when I was first appointed Chairman of the President's Cancer Panel, my colleagues and I visited three important NCI-designated cancer centers in the Nation this year. Panel meetings were held at Columbia University's College of Physicians and Surgeons in New York City, at the Clinical Science Center of the University of Wisconsin in Madison, and at the College of Medicine of the University of Arizona in Tucson. The fourth Panel meeting was held in Bethesda, Maryland, at the National Institutes of Health, to obtain direct reports from the Executive Committee of the NCI.

Together with my comembers on the Panel, Dr. William P. Longmire, Jr., and Dr. John A. Montgomery, I observed and learned of the progress, accomplishments, and problems at the centers. These hearings focused on the most significant and innovative developments in cancer therapy. At each meeting, we learned about progress being made as a direct result of financial support obtained from the National Cancer Program. The reports concerned new developments in radiation treatments, the use of antiviral therapy for AIDS, the therapeutic uses of immunologic stimulative factors, hyperthermia, monoclonal immunotoxins, growth factor antagonists, and successful new approaches to the reversal of drug resistance in human tumors.

In addition to these hearings at NCI-supported cancer centers, the members of your Cancer Panel participate in all meetings of the National Cancer Advisory Board (NCAB), where we are continually apprised of all ongoing and planned programs at the NCI and the organizations and individuals it supports.

In response to your request in June 1988, as head of the Presidential Task Force on Regulatory Relief, the Panel established the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS. This committee is organized to undertake a systematic study of drug regulation as it affects progress in developing and making available therapies for cancer and for AIDS. The committee consists of nine distinguished individuals selected following a nationwide search and is chaired by Dr. Louis Lasagna, dean of the Sackler School of Biomedical Sciences at Tufts University. It is expected that the committee will complete its task and submit its recommendations within 1 year.

Cancer Treatment

The emphasis that is placed on the support of basic or fundamental research by the National Cancer Institute has again proven itself to be the correct policy. Multiple examples of translation of new basic discoveries into applied effective treatments for patients with cancer were reported to the Panel at each of the hearings this year.

Following extensive laboratory and clinical study and development by Dr. Steven A. Rosenberg at the NCI, the technique of adoptive immunotherapy is now being successfully applied to many patients. This therapy was made possible through the cooperation of industry with government research, in providing an adequate supply of pure recombinant interleukin-2 (IL-2). In 1984, prior to this scientific partnership, only 16 patients could be treated with available material. With the new productivity resulting from recombinant DNA technology, it now is possible to effectively treat hundreds of patients.

Patients with advanced melanoma and renal cancer who were not responsive to any other therapy have been treated effectively with the newly available IL-2. White blood cells, called lymphocytes, taken from the patients, are treated with IL-2 in the laboratory and converted into lymphokine-activated killer cells (LAK cells), which can kill cancer cells in patients. Since IL-2/LAK was approved for special use by the FDA last year, 11 cancer centers have treated 122 patients with the therapy.

This year Dr. Rosenberg and his colleagues at the NCI have made an extraordinary advance by isolating and culturing tumor-infiltrating lymphocytes (TILs) from the patients' own tumors. TIL cells are grown with IL-2 in laboratory cultures, and then are reinjected into the patients' bloodstreams. This therapy appears to be almost 100 times more effective *in vitro* in destroying cancer cells than the earlier IL-2/LAK procedure.

This new immunotherapy protocol incorporates the anticancer drug cyclophosphamide, which is thought to enhance the response to the treatment. The initial clinical study, with a small group of patients, resulted in at least a 50-percent reduction of the tumors in 60 percent of the patients. This remarkable response rate is the highest ever reported for the treatment of advanced melanomas.

Following these excellent results, TIL/IL-2 immunotherapy is undergoing clinical trials for other advanced cancers in both children and adults.

Basic research has additionally led to the formulation of a successful new treatment that overcomes the

previous resistance to chemotherapeutic drugs. Quinidine, amiodarone, and verapamil, previously used only for heart disease, have now been found to be effective in reversing the drug resistance of certain cancers and enabling effective drug therapy. The use of of these drugs came about within 1 year of the elucidation of the fundamental blocking mechanism employed by cancer cells.

New basic studies in molecular engineering and recombinant technology have enabled the structuring of molecules capable of seeking and destroying target cells in patients. The new techniques permit monoclonal antibodies to be chemically joined with molecules of potent toxins and to kill specific disease cells in AIDS and cancer patients. Clinical trials with such immunotoxins are being vigorously pursued.

A major effort by the National Cancer Institute is the program for clinical drug development. Phase I clinical trials consist of dose tolerance studies in human patients, and phase II trials are designed to determine the responses of different cancers to the test compounds. In 1988, the NCI entered 24 new drugs and biologicals into phase I clinical trials and supported the evaluation of 97 new medicinals in phase II trials.

Promising compounds that are being studied include trimetrexate, deazaaminopterin, taxol, and a number of colony-stimulating factors, examined alone and in various combinations with other therapeutics.

The phase II trials included tests of fludarabine, which has been very effective for chronic lymphocytic leukemia; two new tumor cell radiation sensitizers, SR-2508 and RO-038799; batracylin, which has shown activity against solid tumors in the laboratory; carboplatin, which is active in humans and less toxic than cis-platin; as well as further studies of IL-2 and TIL cells combined with cyclophosphamide and interferon-alpha. There have been excellent initial responses thus far with these compounds in patients with malignant melanomas or renal cell cancers.

A significant advance in adjuvant therapy has been added to the treatment of breast cancer. A 5-year study involving three separate clinical trials by the National Surgical Adjuvant Breast and Bowel Project (NSABP) headed by Dr. Bernard Fisher, and the Eastern Cooperative Oncology Group (study chaired by Dr. Douglas Tormey), determined that adjuvant hormone therapy or chemotherapy, following surgery, will significantly prolong the disease-free survival rates for women with early breast cancer.

In response to this dramatic finding, the NCI mailed a clinical alert to 13,000 physicians and to professional organizations to enable them to immediately implement these findings as warranted. It is believed that this rapid information transfer will prolong the lives of 10,000 women of the 60,000 diagnosed cases this year alone. Additional technical information was disseminated through the Physicians Data Query (PDQ) system, a computerized, up-to-the-minute NCI information system available to all physicians.

The Panel reconfirmed that in 1988 cancer treatments used in the United States are more effective and less difficult for the patients than ever before. Drugs, biologicals, and irradiation, in combinations and with surgery, have improved the survival results for breast cancer, colon cancer, rectal cancer, prostate cancer, head and neck cancer, and bone and soft tissue sarcomas, as well as the leukemias, lymphomas, and other blood cancers. The advances in cancer treatments have resulted in life-prolonging procedures, accompanied by methods that obviate the need for colostomies, that preserve breasts, that avoid impotence, that preserve limbs, and thus have enhanced the quality of life significantly for cancer patients. During 1988, over 385,000 cancer patients benefitted from the new, less debilitating, successful treatments that have been developed since the National Cancer Act was passed in 1971.

However, the Panel is concerned that the NCI budget for clinical trials has not increased significantly over the past 5 years. Since many exciting new therapies are ready to be tested, the resources are not adequate for the necessary studies.

Molecular Genetics and Oncogenes

The discovery that certain genes, oncogenes, are consistently associated with the development of tumors revolutionized the approach to molecular genetic studies of cancer in the 1980's. Oncogenes are small pieces of genetic material originally isolated from viruses which infect animal cells and produce tumors. Further research revealed that viral oncogenes are identical to certain normal genes in healthy cells. These genes, through messenger RNA, direct the synthesis of proteins that cause neoplastic growth. This gene expression can be suppressed by complementary or "antisense" RNA, which binds to the message, preventing its function and leading to its enzymic destruction, which may result in cell differentiation or death. Antisense messages also have been found to inhibit the growth of the AIDS virus. This research is being vigorously pursued at present.

Research during the last few years has led to the discovery that proto-oncogenes are important in the normal functioning of the cell and are crucial factors in all cell proliferation and organ growth. The oncogenes code for proteins that stimulate cells to divide.

A new group of genes was discovered this year that suppresses the development of cancer cells. These suppressor genes have been identified as anti-oncogenes. Cancer can arise when suppressor genes are lost or inactivated. Certain cancers, such as familial colon cancer, hereditary reti-

noblastoma, and familial bladder carcinoma have now been recognized as caused by mutations of the suppressor genes in the afflicted patients.

There are currently over 40 known oncogenes. Intensive research is presently being conducted to develop molecular structures capable of thwarting the oncogene messages in proliferating cancer cells without impairing normal cells.

Prevention and Control of Cancer

Research on the prevention of cancer is closely interwoven with research on the causation of cancer. Just as the knowledge of genetic defects enables research scientists to design curative treatments, knowledge of the development of cancer will enable researchers to design additional preventive strategies. Cancer causation research and epidemiologic research have identified a wide variety of materials that cause cancers in humans. Cigarettes, chewing tobacco, occupational chemicals, asbestos, viruses, and certain dietary substances have been shown to induce cancers in animals and are associated with higher cancer incidence in humans.

The single most effective way to reduce cancer is to reduce tobacco use. This year the NCI initiated a new strong antismoking program that will reach 10 million people in 25 states. The decrease in lung cancer incidence for adult white males over the past 2 years indicates that educational programs have been effective in this population. A 40-percent reduction in the prevalence of adult male smokers in the United States over the past 20 years is believed to be the reason for the reduction in lung cancer for that population.

Other promising prevention approaches include modifications in the diet since dietary factors may contribute as much as 30 percent to the incidence of certain cancers in the United States. The NCI is studying a number of chemopreventive effects, including additions to food of such items as folic acid/vitamin B_{12}, retinol, 13-cis retinoic acid, beta-carotene, and vitamin E. Certain fruits and vegetables, especially those high in beta-carotene, are believed to have protective effects. Intensive dietary studies are being conducted in Linxian, China, and among special U.S. populations in New Jersey, Louisiana, and Texas.

The NCI, with the concurrence of its scientific advisors, has decided to form a laboratory of human nutrition to learn more about the relationship between the foods we eat and the development and prevention of cancer. The Panel is concerned that the constraints of personnel ceilings and construction funds are preventing the NCI from moving forward with this important initiative.

Information Dissemination

When new methods for cancer prevention become evident, the next crucial step is the dissemination of the research results to health professionals and to the general population. The NCI has built a network for information dissemination over the past decade, which now includes 60 cancer centers throughout the nation. Also included in this network is the International Cancer Research Data Bank, the PDQ computer system, the Community Outreach Program, and the Cancer Information Service (CIS). Both PDQ and CIS can be accessed by anyone in the United States without cost via the 1-800-4-CANCER telephone line. In 1988, the CIS staff responded to over 400,000 telephone inquiries. The Panel notes that the NCI requires additional funds to cover the costs of this valuable service to cancer patients, their families, and the public.

Advances in cancer treatment have enabled the 5-year relative survival rates for all forms of cancer in the U.S. white population to increase from 30 percent to the current level of 50 percent over the past 20 years. However, the 5-year relative survival rate for all cancers in the black population is currently 38 percent. The factors involved in this survival differential are complex, but it is crucial that this information can be disseminated to the black community.

To enhance the dissemination of cancer prevention information and to highlight issues of significance to the public, the NCI and members of the National Cancer Advisory Board developed the National Black Leadership Initiative on Cancer, chaired by Dr. Louis Sullivan. This past year, successful meetings were held in Atlanta, Los Angeles, Chicago, New York, Washington, D.C., and Houston to educate, stimulate, and organize leaders of the black community. The NCI will now support followup activities in cities with large black populations. To further explore the research priorities that could lead to improvement in black cancer survival rates, the NCI has funded 10 programs for $26 million to examine the scientific reasons for the differentials in the black population regarding tobacco use, alcohol, diet, occupation, availability of medical services, use of available health programs, and other cultural or behavioral barriers to improvement in their survival statistics.

Acquired Immunodeficiency Syndrome (AIDS)

The National Cancer Institute has been significantly involved in AIDS research for the past 7 years. The NCI's viral oncology research program included productive efforts in retrovirology and led to the codiscovery of the AIDS virus, HIV-1, by Dr. Robert Gallo. AIDS pathogenesis research continues and NCI scientists now have cloned the genes from the HIV virus and are currently developing systems to interfere

with HIV replication in infected cells.

Recent research has discovered the existence of other human immunodeficiency viruses. An AIDS patient may simultaneously be infected with HIV and another human B-lymphotropic virus (HBLV), which attacks and kills crucial cells of the patient's immune system. These viruses also infect retinal tissue and brain cells, which severely complicates treatment of the disease.

Dr. Samuel Broder first demonstrated the utility of azidothymidine (AZT) for the treatment of AIDS patients at the NCI in 1985. AZT even today remains the only drug licensed for the treatment of AIDS. Since 1985, considerable and increasing efforts have been applied in this area. The drug development program at the NCI currently has three major components to identify and develop effective treatments for AIDS: 1) Large-scale drug screening and development, 2) laboratory-based research in drug design and discovery, and 3) early clinical trials for new agents.

The Office of the Assistant Secretary for Health and the Public Health Service, recognizing the NCI's expertise and established programs for screening and developing anticancer drugs, requested the Institute to create and operate a program for the discovery and development of agents that would be effective against the AIDS virus.

The AIDS Preclinical Drug Screening Program has now been established and is the only one of its kind in the United States. Compounds are accepted for screening from industry, university laboratories, and other government laboratories. The Preclinical Drug Screening Program at the NCI has been mobilized this past year to perform 10,000 tests of new agents, and the staff is improving the techniques to achieve 30,000 assays per year. These tests will involve approximately 15,000 synthetic or naturally occurring compounds at various concentrations, to determine their ability to interfere with viral infection and multiplication in human cells.

During the past year, Dr. Broder and his staff developed a new treatment regimen, alternating AZT with dideoxycytidine (DDC) in patients with severe HIV infections. Alternate weekly treatments with these two drugs have provided sustained suppression of the AIDS viruses, while avoiding the development of major toxicities from either drug.

AIDS can be transmitted from an infected mother to her infant *in utero,* and the NCI is studying the progression of the disease during pregnancy. Pediatric AIDS is an increasing problem in the United States and elsewhere throughout the world. Dr. Philip Pizzo of the NCI's Pediatric Branch has shown that AZT provides a very significant beneficial effect on the neurologic problems which are a major feature of childhood AIDS.

Since AZT remains the most successful drug available for AIDS patients, it has been investigated as cotherapy with a number of other compounds. Promising results are being obtained in NCI-supported studies incorporating colony-stimulating factors, acyclovir, dideoxyadenosine, dideoxyinosine, D-penicillamine, amphotericin B, carbovir, cyclosporin A, castanospermine, foscarnet, and dextran sulfate. These current studies are being vigorously pursued in coordination with the National Institute of Allergy and Infectious Diseases, the coordination center for AIDS research at the National Institutes of Health.

In a special situation, the Panel notes that since President Nixon gave the Cancer Institute the former biological warfare facilities at Fort Detrick in Frederick, Maryland, the NCI has developed an exceptional facility for research on cancer and on AIDS. It houses the Biologic Response Modifier Program, the screening programs for AIDS and cancer drugs, a number of basic science laboratories, the NCI supercomputer, and the AIDS vaccine research program. The Panel is concerned that construction funds needed to maintain this facility, prevent its deterioration, and provide the protection needed to work with the AIDS virus have not been provided in recent years. The investment in this scientific center of excellence, the Frederick Cancer Research Facility, must be protected and maintained.

Conclusions

My colleagues and I on the President's Cancer Panel are more enthusiastic and optimistic in our support of the ongoing programs of the National Cancer Institute than ever before. The continued progress in research and the remarkable advances in treatment obtained in the past year have come about as a result of a well-balanced program and the effective use of funding.

Dr. Vincent T. DeVita, Jr., who had been the Director of the National Cancer Institute for the past 8 years, is to be praised and credited for his extraordinary leadership, which made possible the outstanding progress in cancer research we have witnessed. We feel confident that Dr. Samuel Broder, the newly appointed Director of the NCI, will establish initiatives and provide the leadership to continue and expand the new opportunities for progress of the National Cancer Program.

There are many reasons to take pride in the important achievements of the National Cancer Program. These range from new insights into the biological processes at the molecular level of the cell, to the establishment of a network of medical centers and community oncology groups which stretch across the Nation. However, I still feel a terrible sense of urgency. Despite many major achievements, hundreds of thousands of people die each year of cancer. Furthermore, despite rapid progress in cancer research, and reasonably effective efforts at its prevention, because of the aging of the American population, cancer will soon become the number one killer in the United States.

In 1971 only 35 percent of patients were cured of cancer. Today half of all cancer patients can be cured. Since 1971, when the National Cancer Act

was passed, numerous wise decisions have been made to invest in both basic research efforts and in specific programs to apply the results of that basic research. The Congress and the American people made a correct, far-sighted investment in cancer research, which now saves 150,000 more lives each year than was possible a decade ago.

The Panel must register its concern that recent budget increases for cancer research and training have not been sufficient even to sustain existing activities. In addition, the number of full-time-equivalent positions for cancer research in the Institute has been reduced by 382 since 1984. This impairs the ability of the Institute to exploit new scientific opportunities in cancer as rapidly and as fully as it should, and impedes the progress of the National Cancer Program.

Scientists have vastly increased the knowledge we have about the development of cancer. In the past 2 years the appreciation of the functions of oncogenes and anti-oncogenes has moved us closer to the potential for specific interventions, and eventual total suppression of the diseases called cancer.

The investment in basic research in cancer biology also provided improvements in diagnosis and treatment. Sensitive new diagnostic procedures detect and identify tumors at early stages of development, which increasingly allows physicians to treat patients successfully on effective protocols. The development of biological response modifiers, the incorporation of lymphokines, colony-stimulating factors, and other immunologic factors, have now added a fourth modality to the traditional three used in cancer therapy. Physicians may use surgery, radiation, chemotherapy, and, now, immunotherapy to treat cancer. These innovations in treatment are providing a higher quality of life to individuals for whom there had been no alternatives and no hope just 5 years ago.

It is now crucial to maintain this momentum. Science and medicine can succeed in removing cancer from the list of fearful consequences of life. It requires continued foresight and dedication, as has been demonstrated by this Nation's leaders in the past. Together with my colleagues on the Panel, I urge the Nation to continue this battle to a successful victory.

Chairman

Concur:

William P. Longmire, Jr., M.D.

Concur:

John A. Montgomery, Ph.D.

President's Cancer Panel

National Cancer Program National Cancer Institute

November 1, 1989

The Honorable Dan Quayle
President of the Senate
S-212 Capitol Building
Washington, DC 20510

Dear Mr. President:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute. Section 415(3)(b) of the Health Omnibus Extension Act of 1988 requires that the report be made available to the Congress in addition to the President.

My colleagues on the Panel and I agree that the National Cancer Program is extremely well managed and has produced tangible benefits for cancer victims throughout the country. We feel the continued progress in research and the advances in treatment obtained in the past year have come about as a result of a well-balanced program and the effective use of funding.

However, while we have made major achievements in cancer therapy, hundreds of thousands of people die each year from cancer. Furthermore, despite rapid progress in cancer research and more effective efforts at prevention, cancer — largely because of the aging of the American population — will soon become the number one killer in the United States. We cannot be complacent about this dreadful probability.

The Panel is very concerned that recent budget increases for cancer research and training have not been sufficient to sustain existing activities. Only approximately 25 percent of approved grants will be funded by the National Cancer Institute this year due to budget restraints. This means that almost 75 percent of very good research is not being pursued, research that could possibly lead to the final solution to the cancer problem.

I recognize, of course, that this is a time when government spending must be restrained, but we are in danger of losing the momentum that has been built up with so much effort over the past several years.

In an effort to prevent this from happening, I have established the STOP CANCER campaign, concerning which I have written you previously. I want to put all of our best scientific minds to work on finding a cure for cancer, not just a small percent of them. As you know, I hope to raise $500 million in private funds over the next 4 years for the National Cancer Institute in the hope that matching funds will be provided by the Congress. The campaign is going well, and we have to date raised $12.5 million with only one major fundraising event. I plan to stay in touch with the Congress concerning this campaign.

I hope you will find the attached report of interest.

With best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

President's Cancer Panel

National Cancer Program National Cancer Institute

November 1, 1989

The Honorable George J. Mitchell
Majority Leader
United States Senate
S-221 Capitol Building
Washington, DC 20510

Dear Senator Mitchell:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report to the President which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute.

My colleagues on the Panel and I agree that the National Cancer Program is extremely well managed and has produced tangible benefits for cancer victims throughout the country. We feel the continued progress in research and the advances in treatment obtained in the past year have come about as a result of a well-balanced program and the effective use of funding.

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I hope you will find the attached report of interest in light of the important role you play in health-related matters in the Congress.

With best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

President's Cancer Panel

National Cancer Program National Cancer Institute

November 1, 1989

The Honorable Louis W. Sullivan
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Mr. Secretary:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute. Section 415(3)(b) of the Health Omnibus Extension Act of 1988 requires that the report be made available to the Secretary of Health and Human Services, as well as to the President and the Congress.

My colleagues on the Panel and I agree that the National Cancer Program is extremely well managed and has produced tangible benefits for cancer victims throughout the country. We feel the continued progress in research and the advances in treatment obtained in the past year have come about as a result of a well-balanced program and the effective use of funding.

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With best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

President's Cancer Panel

National Cancer Program National Cancer Institute

November 1, 1989

The Honorable Tom Foley
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 which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute. Section 415(3)(b) of the Health Omnibus Extension Act of 1988 requires that the report be made available to the Congress in addition to the President.

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With best wishes,

Sincerely,

Armand Hammer

Chairman

Attachment

Attachment M

Report of the Chairman to the President,

January 1 to December 31, 1989

January 1 to December 31, 1989

President's Cancer Panel

Report of the Chairman

U.S. Department of Health and Human Services

Public Health Service

National Institutes of Health

National Cancer Institute

NIH Publication
No. 90-3179
August 1990

President's Cancer Panel

National Cancer Program National Cancer Institute

Chairman:
Dr. Armand Hammer
Occidental Petroleum Corporation

Dr. John A. Montgomery
Southern Research Institute

Dr. William P. Longmire, Jr.
Center for the Health Sciences
University of California, Los Angeles

Executive Secretary:
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20892
Telephone: 301-496-1148

August 15, 1990

The President
The White House
Washington, D.C. 20500

Dear Mr. President:

The Health Omnibus Extension Act of 1988 requires the Chairman of the President's Cancer Panel to submit a report to you each year on the status of the National Cancer Program. Accordingly, I am pleased to submit my report for 1989 as attached.

My colleagues on the Panel, Dr. William P. Longmire and Dr. John A. Montgomery, agree that the National Cancer Institute's programs are well established and productive. We feel that major treatment advances have evolved from NCI-funded intramural and extramural research programs. Indeed, oncologists now have a fourth form of cancer therapy available due to the innovative work performed by Dr. Steven A. Rosenberg and his colleagues. In addition to the traditional treatment forms of surgery, radiation, and chemotherapy, we now have immunotherapy, which utilizes the body's own defense mechanism — the immune system — to fight cancer.

Recently, Dr. Rosenberg and his colleague at NCI, Dr. Michael Blaese, together with Dr. French Anderson of the National Heart, Lung, and Blood Institute, made history in furthering the understanding of tumor-infiltrating lymphocyte (TIL) therapy. They transferred a "foreign" nonhuman gene into a human patient to serve as a marker for tracking TIL cells in the body. Early results of this gene transfer are gratifying. The TIL treatment itself has improved the status of a number of patients so treated, all of whom had malignant melanomas and had not been expected to live past three months. Gene transfer research lays the groundwork for future therapeutic methods, potentially initiating an entirely new era in medicine for the correction of inherited diseases.

A further indication of the benefits achieved from the work of the National Cancer Institute lies in statistics showing that in 1980 cancer mortality was decreasing for Americans under 50; it has now been advanced to patients under age 65.

The scientific and technological discoveries of this past year were true harvests derived from wise investments made by the Federal government in the National Cancer Program. The Director of that Program, Dr. Samuel Broder, has contributed strongly and effectively to the furtherance of science and the achievement of outstanding clinical results.

Nevertheless, we on the Panel feel there is a renewed sense of urgency to redouble our efforts to ensure that all Americans, regardless of race or ethnic background, share equally in the benefits that are derived from the latest advances in cancer prevention and treatment, both now and in the future.

The legally mandated NCI By-Pass Budget describes specific funding requirements that would provide this Nation with the ability to capitalize on scientific opportunities in cancer research and could markedly reduce deaths from cancer within this decade. An Executive Summary of the 1992 By-Pass Budget is attached. The Panel strongly endorses its proposals. I understand the complete document, noting program accomplishments and future plans, is being provided to your office separately. We hope that this professional needs budget will be helpful in guiding you in preparing the FY 1992 budget. With sufficient resources it is my firm belief that we can make even stronger advances towards eradicating this disease.

I would also like to report, Mr. President, that my STOP CANCER Campaign continues to move forward. I was able to present the NCI with $5 million earlier this year and expect to provide an additional $7.5 million before the year is out, which will match the $12.5 million authorized by the Senate Appropriations Subcommittee specifically as a result of the STOP CANCER Campaign. These additional funds will be used by the NCI to support high-quality innovative research.

I would like to thank you for the privilege of serving as Chairman of your Cancer Panel. Your continued support for the programs of the NCI has permitted the Institute to continue the excellent work they are undertaking. I hope the attached report will prove useful to you and others in your Administration in planning for the future. As always, you have my great admiration for your accomplishments, both domestic and international, and for the inspired leadership you provide to all Americans.

Respectfully,

Chairman

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Attachments

1989 CHAIRMAN'S REPORT TO THE PRESIDENT

During 1989 the members of the President's Cancer Panel conducted hearings at institutions in the United States where the National Cancer Program is being implemented. We also participated in all meetings of the National Cancer Advisory Board held at the National Institutes of Health in Bethesda, Maryland. The Panel was witness to remarkable progress in cancer research throughout the country in various aspects of cancer prevention, diagnosis, and treatment. The Panel also recognized that addressing the cancer problem in minority and underserved populations requires serious attention and additional support.

In 1989 we continued the approach I initiated in 1981, at the time of my first appointment as Chairman of the President's Cancer Panel. My colleagues Dr. William P. Longmire and Dr. John A. Montgomery and I have held meetings at three institutions that conduct research training and cancer control activities supported by the National Cancer Institute (NCI). Dr. Samuel Broder, Director of the NCI, participated with us in these meetings, which were held at Howard University in Washington, D.C., at Meharry Medical College in Nashville, Tennessee, and at Stanford University in California.

At the Howard University Cancer Center, Dr. Kenneth Olden, Director, reported on specific black cancer research issues, and the Commissioner of Public Health for Washington, D.C., Dr. Reed Tuckson, described the issues surrounding the high incidence and mortality of cancer in blacks.

Dr. David Satcher, President of Meharry Medical College, told the Panel about the new Drew-Meharry-Morehouse Cancer Consortium, which is designed to concentrate its unified strength on the problems of cancer in black populations. This NCI-supported center will enhance training, education, and community involvement in areas of maximum need.

The Panel meeting at Stanford University concentrated on biomedical training and technology transfer. Dr. David Korn, Vice President and Dean of the School of Medicine, provided the Panel with an excellent case study of the commercial development of laboratory findings by an amalgam of private capital, university facilities, and federally supported basic research. Such development promotes the rapid transfer of research findings to applications for cancer treatment and diagnosis.

The final meeting of the year was held in Bethesda, Maryland, to hear reports from the Assistant Secretary for Health, DHHS, the Commissioner of the Food and Drug Administration (FDA), and the NCI staff.

The Institute researchers told the Panel about new drugs used to treat certain cancers and the use of gene-modified cells in cancer immunotherapy. FDA Commissioner Frank Young provided details about new collaborative programs at the FDA and the NCI, and Assistant Secretary for Health, Dr. James Mason, delivered an excellent overview of health research from the national perspective.

Cancer Prevention

The National Cancer Institute and the National Cancer Program are dedicated to generating knowledge and applying it quickly. They constitute the Nation's response to the challenge of cancer: a million new cases diagnosed each year and the loss of a half-million lives. We on the Panel believe it would be much worse had the NCI's efforts not been so successful to date.

Currently, there are more opportunities for research projects than there are funds available to support them, and more tasks than there are staff to perform them. NCI's programs are well established and productive. Successful research requires not only creative and skilled scientists, but well-equipped laboratories. We must prevent erosion in our cancer centers, each of which is a major resource to the community it serves, and to the Nation.

Estimates are that two-thirds of all cancers may be linked to lifestyle. Reducing the morbidity and mortality from cancer during this decade will likely rest on one lifestyle change: reduction of smoking. To meet this challenge, NCI has signed a cooperative agreement with the American Cancer Society to carry out a major smoking reduction program called the American Stop Smoking Intervention Study, or ASSIST/2000.

ASSIST/2000 is a demonstration project that will be the largest program in tobacco-use prevention and cessation in the world. It will reach more than one-fifth of the U.S. population, including at least 15 million smokers in large metropolitan areas, towns, or entire states. Intervention approaches will be employed in randomized trials such as school-based programs, self-help strategies, physician/dentist-delivered interventions, mass media approaches, and community-based interventions.

The value of screening mammography has been clear for well over two decades. Low-cost mammograms are available as part of special campaigns to detect cancer. Yet only 17 percent of women 40 years of age and over have ever had mammograms. The reasons that women do not seek mammograms generally relate to issues such as finances, fear, and pessimism rather than to a lack of information

about the value of early detection of small tumors.

The NCI has initiated a National Breast Screening Awareness Campaign employing mass media materials and physician and patient education to encourage mammography use for early detection. A Women's Leadership Summit on Mammography was held last fall on Capitol Hill to launch this campaign. First Lady Barbara Bush gave the keynote address encouraging women to put mammography on their personal and professional agendas.

The Pap test, another well-established screening test, is also underused. It is estimated that 6,000 women will die this year of cervical cancer despite the fact that the Pap test is almost universally available and can detect precancerous changes in the early curable stage of this cancer. Women must be encouraged to have this test performed.

The National Cancer Institute has undertaken other cancer prevention research. NCI-supported chemopreventive clinical trials are testing methods to inhibit the development of cancer with various substances such as vitamins and micronutrients. Some studies are focused on high-risk individuals such as testing the preventive effects of beta-carotene and retinol for asbestos workers. Another trial is evaluating the preventive role of dietary fiber and calcium in individuals who have a high risk of colon cancer.

A recent NCI-supported study indicated that a high wheat-fiber supplement given to patients with familial adenomatous polyposis decreased the number of precancerous polyps. This is an exciting finding and can lead to significant advances in the prevention of colorectal cancer.

Various clinical results reaffirm the principle that real gains in reducing cancer incidence and mortality will ultimately come from prevention strategies. Earlier efforts at prevention were aimed at eliminating exposure to carcinogens and identifying early lesions. Recent new understanding of genetic events that lead to cancer has stimulated sophisticated interventions in patients with inherited cancer-receptive defects.

The NCI's primary focus in the Cancer Prevention Research Program is to develop, evaluate, and disseminate successful strategies for the control and prevention of cancer. This has been implemented by the Community Clinical Oncology Program (CCOP), which includes research trials in cancer treatment, cancer control, and research into cancer prevention. During 1989 there were 52 community programs initiated in 30 states, involving over 2,000 physicians.

In the review conducted by the Panel it was recognized that this program has been extremely successful, particularly in the area of clinical trials accrual, and should indeed be doubled to cover all states and reach at least 100 communities in the Nation.

Cancer Treatment

Major treatment advances have evolved from NCI-funded intramural and extramural research programs. The seminal work in immunotherapy has added a fourth treatment modality to the traditional ones of surgery, radiation, and chemotherapy. This treatment uses various "host cells" of the patient that are enhanced in the laboratory and then reinjected into the patient to fight the patient's tumor.

Recently, two NCI scientists, Drs. Steven Rosenberg and Michael Blaese, together with Dr. French Anderson of the National Heart, Lung, and Blood Institute, made history in furthering the understanding of tumor-infiltrating lymphocyte (TIL) therapy. They transferred a "foreign" nonhuman gene into a human patient to serve as a marker for tracking TIL cells in the body. Enhanced TIL cells kill tumor cells while sparing normal cells.

Early results of this gene transfer are gratifying. The genes were transferred on May 22, 1989, and the TIL cells with those transferred genes have remained active in some patients. The TIL treatment itself has improved the status of a number of the patients, all of whom had malignant melanomas and had not been expected to live past three months.

Additional NCI research on biological response modifiers has produced very exciting early clinical results in otherwise untreatable cancers. The gene transfer research lays the groundwork for future therapeutic methods, potentially initiating an entirely new era in medicine for the correction of inherited diseases.

Clinical treatment research expands upon promising leads developed in preclinical research and evaluates new treatments in patients with cancer. Clinical trials consist of three phases. Phase I trials establish the maximum dose tolerated and provide information on side effects encountered with the new therapy. Phase II trials examine the efficacy of the new drug for various types of cancer. Phase III trials compare the new treatment with the best previously known therapy.

The development of resistance to chemotherapeutic agents remains a great obstacle to complete tumor eradication and long-term disease-free survival. One of the most intensively studied examples of this phenomenon is multidrug resistance, characterized by resistance to a wide variety of diverse drugs following exposure to only one of them. It has been discovered that multidrug resistance by cancer cells is caused by overactivity of a "drug pump" called pgp (p-glycoprotein pump). In new experiments, some common drugs such as verapamil, quinidine, and others have been shown to block the function of this pump, resulting in a reversal of multidrug resistance. Clinical trials are now being conducted that combine chemotherapy with pgp-blocking agents.

Last year the Arizona Cancer Center reported the first trial involving patients who had tumors expressing pgp. Patients had developed newly progressive disease while receiving a treatment protocol containing vincristine, doxorubicin, and dexamethasone. When verapamil was added to the protocol, three of eight patients responded positively. Research in this area is being pursued intensively at a number of NCI-supported clinical centers.

The NCI maintains a vigorous program for new drug development in its search for drugs and biologics against cancer. A number of new agents have reached clinical use. Suramin, a drug long used for treating parasitic infections, is being evaluated in patients with advanced prostate cancer. It provides some significant responses in prostate cancers that have progressed to a metastatic stage not responsive to hormonal therapy.

This year the FDA approved Group C status for two important anticancer drugs. Group C status for investigational new drugs is conferred when NCI proves a compound to be safe and effective for treating certain cancers. In May 1989, the NCI also received FDA approval to add the drug combination of levamisole plus 5-fluorouracil (5-FU) for use in the adjuvant treatment of colon cancer.

This combination therapy reduced mortality from Stage III (Dukes' C) colon cancer by as much as one-third, and can affect the lives of about 400 patients per month.

Deoxycoformycin was also approved by the FDA for Group C this past year, and can now be made available to physicians for appropriate patients. New drug approvals for marketing were given for ifosfamide, flutamide, and carboplatin. Ifosfamide is used to treat refractory metastatic testis cancer; flutamide has been effective in treating metastatic prostate cancer; and carboplatin has produced significant positive effects in refractory metastatic ovarian cancer.

At your request, President Bush, the Panel established the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS to identify methods to streamline the FDA drug approval process. This committee of nine extremely competent and dedicated citizens has been holding hearings to develop recommendations regarding the issues you posed as head of the Presidential Task Force on Regulatory Relief. Dr. Louis Lasagna, Dean of the Sackler School of Biomedical Sciences at Tufts University, is the Chairman of the group. Upon completion of the committee's final report, it will be submitted to your office.

For the past 17 years the National Cancer Act has fostered cancer treatment research. Cancer mortality in children declined 36 percent between 1973 and 1987, which is recognized as being due to treatment, particularly through the Nation's network of clinical trials and cancer centers. Mortality rates among persons under age 65 have markedly decreased for many forms of cancer. For patients under age 65, the overall mortality rate for all cancers combined decreased 4.5 percent between 1973 and 1987.

However, the incidence of new cancer cases such as melanoma and non-Hodgkin's lymphoma, breast cancer, and lung cancer in women continues to rise. Mortality rates have declined for other cancers, including uterine corpus and cervix, urinary bladder, thyroid, stomach, ovary, oral cavity, leukemia, colon and rectum, pancreas, brain, and nervous system. Cancer deaths in young adults have decreased greatly. Mortality rates for testicular cancer and Hodgkin's disease have declined by more than 50 percent since 1973.

Bladder cancer mortality has decreased 32 percent; ovarian cancer by 25 percent; colorectal cancer by 15 percent; oral cancer by 20 percent; cervical cancer by 39 percent; and cancer of the corpus uteri by 37 percent.

Other cancers have shown increases: lung and bronchus, 15 percent; melanoma, 16 percent; multiple myeloma, 7 percent; and esophageal cancer, 5 percent.

In the nine years that mark my tenure as Chairman of your Cancer Panel, I have witnessed the impressive advance in the age groups that have benefited from achievements of the National Cancer Program. In 1980 cancer mortality was decreasing for Americans under age 50; it now has been advanced to patients under age 65. This milestone is a tribute to the combination of new basic research, technology transfer, and innovations in cancer treatment.

For persons 65 years of age and older, the overall cancer mortality rate has increased. Some common cancers have shown declines, including colorectal cancer, 7 percent; bladder cancer, 20 percent; and cervical cancer, 40 percent. Other sites have shown increased mortality: lung cancer, up by 53 percent; melanoma by 55 percent; brain cancer by 58 percent; non-Hodgkin's lymphoma by 40 percent; multiple myeloma by 33 percent; breast cancer by 12 percent; and prostate cancer by 8 percent. When 1987 is compared with 1973 for all sites combined, there has been a 13 percent increase in mortality for individuals 65 and older compared to a 21 percent increase in cancer incidence over that 15-year span.

It is estimated that 1,040,000 Americans will be diagnosed with cancer in 1990, and approximately 510,000 people will die of cancer during the year. These projected estimates are based on an increase in the number of older Americans who are at higher risk for developing the disease; half of U.S. cancer cases occur in persons over 67 years of age.

Cancer Etiology

Several forms of cancer appear to develop in at least two steps: the initiation stage and one or more promotion stages. The initiation stage involves an interaction with the cellular DNA so as to alter some gene functions. Initiators include chemicals, fibers, radiation, and viruses. Nutritional, hormonal, environmental, and genetic factors can act as promoters, which do not cause cancer directly, but facilitate the process.

Research this year in animals and in vitro characterized the products of carcinogen-DNA interactions that are termed "adducts." Sensitive immunologic techniques employing new antibodies were developed to detect adducts in individuals exposed to various environmental carcinogens. Such adducts may be useful as indicators of exposure to carcinogens that occurred many years previously.

In contrast to tumor initiators, tumor promoters do not appear to interact with DNA. They act by modulating gene expression, cell differentiation, and growth. Several chemicals have been found to act as antipromoters in a laboratory model system, which suggests these agents may be useful to prevent cancers in humans.

Biological carcinogenesis research examines the mechanisms of carcinogenesis involving biological agents, viruses, and genes at the cellular and molecular levels. It has been found that cancer may occur either through the direct effects of viral transforming genes entering cells or indirectly through an initial interaction with environmental factors such as chemicals, radiation, alcohol, and dietary components followed by genetic modifications of cells.

Research regarding viral oncogenes, cellular proto-oncogenes, and suppressor genes is being vigorously pursued, and continues to provide fundamental information about the development of human cancer.

Acquired Immunodeficiency Syndrome (AIDS)

The National Cancer Institute conducts AIDS research as an extension of its viral cancer research program and its drug development program and has a significant role in AIDS drug and vaccine development.

During the past decade, NCI established a comprehensive Preclinical AIDS Drug Screening Program, now capable of testing well over 10,000 new compounds per year for activity against the human immunodeficiency virus (HIV). Azidothymidine (AZT), still the only agent proven to prolong the lives of AIDS patients, was developed at the NCI in collaboration with the Burroughs Wellcome Company. Several other agents that inhibit HIV in cell culture are in clinical development. The NCI AIDS Vaccine Task Force is pursuing a coordinated approach to the development of an effective AIDS vaccine. During the past decade, NCI has devoted major efforts to investigating the exact biologic mechanisms by which HIV causes infection, immune system destruction, multiorgan system dysfunction, and some HIV-related cancers. NCI has also undertaken several epidemiologic and natural history studies, both descriptive and interventional, in the United States and abroad. These studies aim to determine the time course of HIV infection and of overt disease, to identify the major risk factors for acquiring HIV, and then to design competent strategies to interrupt these processes. This research is presently yielding valuable information.

The NCI AIDS drug development program includes three basic components: a high-capacity drug screen to assess compounds for activity against the HIV virus; a laboratory-based effort for developing novel approaches to drug treatment; and a program for preclinical and early clinical development of drugs with promising anti-HIV activity.

Sixteen drugs moved through the program in 1989 and have reached early clinical studies for antiviral therapy. In addition to the development of AZT, NCI has a number of promising new compounds under clinical development, including dideoxycytidine (ddC), dideoxyinosine (ddI), and fluorinated versions of these drugs. The concept of multimodality or combination therapies, such as those used in cancer treatment, offers promise for AIDS treatment as well.

The FDA recently has made ddI available under a Treatment IND to individuals who are not in clinical trials. Essentially, the guidelines will allow treatment with ddI for patients who are not able to benefit from AZT and who are not eligible for clinical trials.

The NCI has also been involved in the development of agents for opportunistic infections, including trimetrexate for the treatment of *Pneumocystis carinii* pneumonia, a frequent threat to the lives of AIDS patients. The search continues for various laboratory and animal models for clinical testing of drugs and treatment approaches in AIDS research.

Tumor Biology and Molecular Genetics

Tumor biology research supported by the National Cancer Institute has made significant progress in the analysis of tumor cells. It has become more evident that cancer is a disease involving genetic changes in normal somatic cells.

Several years ago, it was found that DNA from tumor cells contains cancer-causing genes called oncogenes that can transform a normal cell to a malignant one. Oncogene research has shown that the cancer cells contain mutated versions of normal cellular genes that are responsible for the abnormal cell growth and behavior associated with cancer. These discoveries have led to new and testable

theories regarding cancer causation and to new approaches to cancer prevention, diagnosis, and treatment. Dr. J. Michael Bishop and Dr. Harold E. Varmus received the Nobel Prize this past year for their research on oncogenes, which was supported by the NCI.

A second group of cellular genes important in oncogenesis has been revealed by studies of the familial inheritance of cancer. These genes are called antioncogenes or suppressor oncogenes, because they suppress the development of cancer. The absence of the gene product rather than its presence is responsible for transformation of normal cells to cancer cells. One example of a suppressor oncogene is the Rb gene, which if lost or inactivated leads to the development of retinoblastoma, a tumor of the eye in young children. The product of another oncogene, called p53, has been successfully used this past year to inhibit cancerous transformation. This research is being intensively pursued in NCI-supported laboratories throughout the country.

Conclusions

My colleagues and I have examined the National Cancer Program in depth across the Nation. We have reviewed the basic research programs, the clinical applications, the progress in prevention and control efforts, the initiation of new minority awareness programs, and the overall progress toward elimination of the diseases collectively called cancer. As Chairman of the President's Cancer Panel, I recognize that our regional meetings, as well as the meetings held in Bethesda by the National Cancer Advisory Board, have provided a heightened awareness of the diversity of the problems. The scientific and technological discoveries of this past year were true harvests derived from wise investments made by the Federal government in the National Cancer Program. It is my view that Dr. Samuel Broder, the excellent Director of that National Program, whom you appointed in January 1989, is contributing strongly and effectively to the furtherance of science and the achievement of outstanding clinical results.

Almost $600 billion is spent annually on medical care in the United States, and much of that cost is borne by the Federal government. Only medical research will provide effective methods to conquer the diseases that cause those expenditures. The National Cancer Program represents an investment for the good of the American people. I therefore feel that this Nation should commit three times its present investment to health research, which is now less than two percent of the cost of medical care.

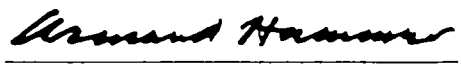
A decade of neglect of our Nation's physical facilities for cancer research and medical education has created a dire need for replacement and modernization in the laboratories and hospitals throughout the country.

The cancer mortality rates in the overall U.S. population could be cut in half using established technologies in cancer prevention and treatment. Minority and underserved populations must receive the benefits of these technologies. Clinical advances must be delivered rapidly throughout the Nation to all populations.

We on the Panel feel there is a renewed sense of urgency to redouble our efforts to ensure that all Americans, regardless of race or ethnic background, share equally in the benefits that are derived from the latest advances in cancer prevention and treatment, both now and in the future.

The legally mandated NCI By-Pass Budget request describes specific funding requirements that would provide this Nation with the ability to capitalize on scientific opportunities in cancer research and could markedly reduce deaths from cancer within this decade. An Executive Summary of the 1992 By-Pass Budget is appended to this report. The Panel strongly endorses its proposals.

This report has been prepared with the cooperation and approval of my colleagues on the President's Cancer Panel, William P. Longmire, Jr., M.D. and John A. Montgomery, Ph.D.



Chairman

President's Cancer Panel

National Cancer Program National Cancer Institute

August 20, 1990

The Honorable Dan Quayle
President of the Senate
S-212 Capitol Building
Washington, DC 20510

Dear Mr. President:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report to the President which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute. Section 415(3) (b) of the Health Omnibus Extension Act of 1988 requires that the report be made available to the Congress in addition to the President.

My colleagues on the Panel, Dr. William P. Longmire and Dr. John A. Montgomery, agree that the National Cancer Institute's programs are well established and productive. We feel that major treatment advances have evolved from NCI-funded intramural and extramural research programs.

One of the most significant developments of the past year involves tumor-infiltrating lymphocyte (TIL) therapy, which seeks to utilize the body's own defense mechanism—the immune system—to seek out and destroy cancer cells. Dr. Steven Rosenberg of the NCI, who initially developed the TIL therapy, and his colleague Dr. Michael Blaese, together with Dr. French Anderson of the National Heart, Lung, and Blood Institute, made history in furthering the understanding of TIL therapy. They transferred a "foreign" nonhuman gene into a human patient to serve as a marker for tracking TIL cells in the body. Early results of this gene transfer are gratifying. The TIL treatment itself has improved the status of a number of patients so treated, all of whom had malignant melanomas and had not been expected to live past three months. Gene transfer research lays the groundwork for future therapeutic methods, potentially initiating an entirely new era in medicine for the correction of inherited diseases.

A further indication of the benefits achieved from the work of the National Cancer Institute lies in statistics showing that in 1980 cancer mortality was decreasing for Americans under 50; it has now been advanced to patients under age 65.

In spite of advances which have been achieved, we on the Panel feel there is a renewed sense of urgency to redouble our efforts to ensure that Americans, regardless of race or ethnic background, share equally in the benefits that are derived from the latest developments in cancer prevention and treatment, both now and in the future.

The legally mandated NCI By-Pass Budget describes specific funding requirements which would provide this Nation the ability to capitalize on scientific opportunities in cancer research and could markedly reduce deaths from cancer within this decade. An Executive Summary of the 1992 By-Pass Budget is attached. The Panel strongly endorses its proposals.

My colleagues and I hope that you will find the attached report useful.

Sincerely,

Chairman

AH:ec

Attachments

President's Cancer Panel

National Cancer Program National Cancer Institute

Chairman:
Dr. Armand Hammer
Occidental Petroleum Corporation

Dr. John A. Montgomery
Southern Research Institute

Dr. William P. Longmire, Jr.
Center for the Health Sciences
University of California, Los Angeles

Executive Secretary:
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20892
Telephone: 301-496-1148

August 20, 1990

The Honorable George J. Mitchell
Majority Leader
United States Senate
S-221 Capitol Building
Washington, DC 20510

Dear Senator:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report to the President which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute.

My colleagues on the Panel, Dr. William P. Longmire and Dr. John A. Montgomery, agree that the National Cancer Institute's programs are well established and productive. We feel that major treatment advances have evolved from NCI-funded intramural and extramural research programs.

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My colleagues and I hope that you will find the attached report useful in view of your special responsibility in the Congress in the area of health and human services.

Sincerely,

Chairman

AH:ec

Attachments

President's Cancer Panel

National Cancer Program National Cancer Institute

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Occidental Petroleum Corporation

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Southern Research Institute

Dr. William P. Longmire, Jr.
Center for the Health Sciences
University of California, Los Angeles

Executive Secretary:
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20892
Telephone: 301-496-1148

August 20, 1990

The Honorable Louis W. Sullivan
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Mr. Secretary:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report to the President which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute. Section 415(3) (b) of the Health Omnibus Extension Act of 1988 requires that the report be made available to the Secretary of Health and Human Services, as well as the President and the Congress.

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My colleagues and I hope that you will find the attached report useful in view of your special responsibility.

Sincerely,

Chairman

AH:ec

Attachments

President's Cancer Panel

National Cancer Program National Cancer Institute

August 20, 1990

The Honorable Thomas S. Foley
Speaker of the House
United States House of Representatives
Capitol Building H-204
Washington, DC 20515

Dear Sir:

As Chairman of the President's Cancer Panel, I am pleased to enclose a copy of the report to the President which I have prepared on the status of the National Cancer Program as operated by the National Cancer Institute. Section 415(3) (b) of the Health Omnibus Extension Act of 1988 requires that the report be made available to the Congress in addition to the President.

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Sincerely,

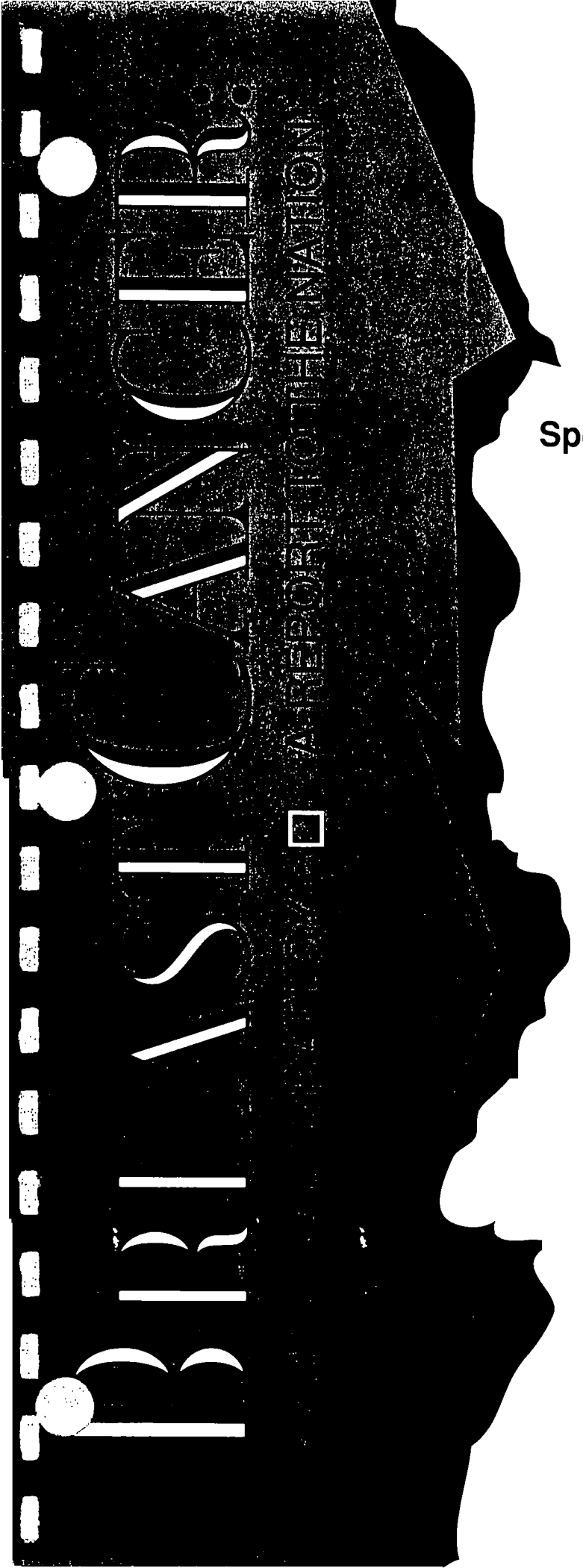
Chairman

AH:ec

Attachments

Attachment N

Breast Cancer: A National Strategy --
A Report of the Nation



The President's Cancer Panel
Special Commission on Breast Cancer

NATIONAL INSTITUTES OF HEALTH
National Cancer Institute

PRESIDENT'S CANCER PANEL

National Cancer Program • National Cancer Institute

Chairman
Harold P. Freeman, M.D.
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PHONE: 301-496-1148
FAX: 301-402-1508

October 29, 1993

Dear Colleague:

We are very pleased to be able to send you the final report of the President's Cancer Panel Special Commission on Breast Cancer.

Over a 15-month period, the Commission members, who are listed in the Appendices to the Report, heard testimony from over 190 speakers on all aspects of breast cancer. Topics the speakers addressed included research in basic science, epidemiology, treatment and prevention, detection and early diagnosis, rehabilitation, and quality of life; the role of industry in developing new products for diagnosis, prevention and treatment; education and information dissemination for patients, the public, and health care professionals; health care delivery and the role of the payers; the contribution of patient advocacy and volunteer organizations; and public policy and legislation. The report also contains a special section on issues for minority and underserved women.

We believe the Commission Members have done a superb job of condensing an enormous amount of information into a set of concise findings and balanced recommendations.

We think this report will be highly valuable to all of us who are committed to the fight against breast cancer. We hope you will find it useful in setting future directions and priorities in our common effort to combat this disease and to reduce the suffering of all too many women in this country, their families, and their friends.

Nancy G. Brinker

Mrs. Nancy Brinker
Chairman
Special Commission on Breast Cancer

Harold P. Freeman

Dr. Harold Freeman
Chairman
President's Cancer Panel

Table of Contents

Executive Summary

Overview

Breast cancer is a large and growing public health problem in the United States. During the decade of the 1990s, it is estimated that nearly 2 million women will have been diagnosed with the disease and that 460,000 women will have died of it. Between 1950 and 1989, the incidence of breast cancer increased by 53 percent. The magnitude of this problem and its constant increase over time understandably result in considerable anxiety among all women.

Some improvements in breast cancer detection and treatment have occurred over the past few decades. Yet even these modest improvements are not uniformly applied throughout the population. Most current therapies (surgery, radiation therapy, and chemotherapy) are non-specific in their effects and frequently diminish quality of life. Although women diagnosed with early-stage breast cancer have a 5-year survival rate of 93 percent, there is no period of time after which a woman who has been treated for breast cancer can be assured that it will not recur. At this time, there are no proven methods of preventing breast cancer.

Advances in basic science have raised the realistic hope that more specific methods can be developed to treat or prevent breast cancer.

Breast cancer advocates – women with breast cancer, their families, friends, and supporters – demand that breast cancer become a national priority. There is a widespread sense of urgency that more can and must be done to address the problem of breast cancer in this country. There is growing public demand for even greater levels of funding of a national breast cancer program and an outcry for the development of cure and prevention.

Recommendations

The goals of the President's Cancer Panel Special Commission on Breast Cancer recommended breast cancer program are:

1. To make substantial progress in developing effective methods to cure and to prevent breast cancer, and

2. To make current and future proven methods of early detection, treatment, and prevention universally available.

The National Institutes of Health and other involved federal agencies must receive research funding of no less than $500 million per year for this program until these goals are achieved.

Specific recommendations made by the commission are outlined below.

Causes and Prevention

- Research into breast cancer causes and prevention must receive high priority.
- Investigator-initiated inquiry should remain the mainstay of research funding.
- Genetic, hormonal, environmental, dietary, and other causes of breast cancer must be identified through basic and epidemiologic research; this knowledge is the foundation needed to develop effective preventive strategies.
- Knowledge gained through research must be translated into clinically effective methods of prevention, early detection, and treatment.

Earlier Detection and Diagnosis

- Early detection should be improved by further refining x-ray mammography, developing newer imaging methods using non-ionizing radiation, and identifying breast cancer biomarkers that can be detected in a blood test.
- Improved access to early detection must include prompt diagnostic work-up and treatment referral for patients in whom breast abnormalities are identified.

Treatment Strategies

- Women must be empowered to be active participants in their decisions about breast cancer screening and, if diagnosed with the disease, about their treatment options.
- Patients, their families, and breast cancer experts want and deserve less invasive, disfiguring, and toxic treatments than surgery, radiation, and chemotherapy.
- High priorities for new and more specific treatments include: therapy directed at hormones and hormone receptors, tumor growth factors or growth factor receptors; inhibitors of angiogenesis and metastasis; immunologic therapy; and gene therapy.
- Methods should be developed to overcome resistance to hormonal and chemotherapeutic agents.
- Diagnostic decisions, treatment options, and recommendations should be provided in an interdisciplinary setting.

Psychosocial Effects

- Current methods of psychosocial support should be available to all breast cancer patients and their families.
- More effective supportive care interventions for breast cancer patients and their families must be developed.

Access

- Current and future methods of early detection, treatment, and prevention should be universally available as soon as their efficacy is demonstrated.
- United States health care delivery system reforms must ensure the removal of financial barriers to access.

- Research is required to understand and remove the non-financial barriers to universal use of effective means of combating breast cancer.

Public Policy

- Federal regulations should limit the proliferation and use of unproven treatments, prognostic markers, prevention methods, and technologies, except within the confines of a well-defined clinical trial.
- Clinical testing of new detection, treatment, and prevention methods should be supported cooperatively by third-party payors, industry, academic centers, and the National Cancer Institute.
- Research costs for clinical trials should be carefully delineated and paid by industry or the National Cancer Institute, while patient care costs should be covered by third-party payors.
- The 1992 Mammography Quality Standards Act should be implemented immediately.
- Federal agencies should coordinate their breast cancer programs through an interagency breast cancer task force.

A Partnership of Breast Cancer Advocates and Breast Cancer Scientists

- This partnership must continue in a way that promotes the shared objective of finding effective prevention and cure of breast cancer.
- Breast cancer advocates should be integrated into decision-making regarding the optimal use of breast cancer research funding.

Information and Empowerment

- Women in the United States should be provided with accurate, up-to-date, and culturally sensitive information about the risks of breast cancer and how it is best detected.
- Women diagnosed with breast cancer should be provided with accurate, up-to-date, and culturally sensitive information about their treatment options.
- The National Cancer Institute should provide leadership in the development and distribution of culturally sensitive breast cancer educational materials and special materials for women with low levels of literacy.
- Women should be empowered both psychologically and financially to take responsibility for their own breast health, including adopting healthy lifestyles, practicing breast self-examination, following recommended guidelines for breast cancer screening, and immediately obtaining diagnostic and treatment services when breast abnormalities are observed.

Past investments in basic science and breast cancer research have brought us to a point where numerous opportunities exist to advance our ability to prevent and treat breast cancer. The enormity of the impact of breast cancer on the mental and physical well-being of women in the United States and their families requires that we as a society devote the resources needed to achieve the most rapid progress possible.

Introduction

Over the last decade, patients and their families have directed increasing national attention to breast cancer. Their input has stimulated breast cancer research, focusing on the need for prevention and cure. During the 1970s and 1980s, breast cancer incidence rose by 21 percent among women of all ages in the United States, and increased by 49 percent among women 65 and older. Even among women least likely to experience breast cancer—those under 50—incidence rose by 13 percent. National Cancer Institute funding for breast cancer has increased from $92.7 million in 1991 to $196.6 million in 1993. In addition, Congress appropriated $210 million to the Department of Defense in Fiscal Year 1993 for a multi-year breast cancer research program. There is wide public demand for even greater levels of funding of a national breast cancer program and an outcry for effective prevention and cure.

In response to a request from the Vice President of the United States to the Chairman of the President's Cancer Panel, the President's Cancer Panel Special Commission on Breast Cancer was appointed by the Director of the National Cancer Institute in 1992. Its 19 members held 11 meetings over 14 months, hearing testimony from more than 190 scientists, clinicians, patient advocates, and experts in all aspects of breast cancer. This report contains the findings and recommendations of the Commission based on this comprehensive review.

Breast cancer is a large and growing public health problem in the United States. All women are at considerable risk for developing breast cancer during most of their lives. It is estimated that during the 1990s nearly 2 million women in the United States will be diagnosed with the disease and that 460,000 women will die of it. Between 1950 and 1989, the incidence of breast cancer increased by 53 percent. Expanded use of screening mammography explains part of the recent rise in incidence, but the causes of the long-term increase are largely not known. The increasing magnitude of this problem has understandably resulted in considerable anxiety in the population, particularly among young women and especially regarding future generations of females.

Specific points about breast cancer should be recognized. The incidence of breast cancer rises continuously as women age: At age 30-34, the rate is 27 per 100,000; at 40-44, it is 127 per 100,000; at 50-54, it is 222 per 100,000; at 60-64, it is 343 per 100,000; and at 70-74, it is 434 per 100,000 women. Also, the natural history of the disease is prolonged. The time from the inception of breast cancer to its detection using current methods is estimated to be at least several years. The time following initial diagnosis and treatment to the development of recurrence and death is measured in years. Furthermore, there is no time period beyond which recurrence and death may not occur. If a cure is defined as elimination of any chance of recurrence and metastases, it is not correct at present to describe a "cure" of the disease. Nevertheless, most patients diagnosed with breast cancer live out the remainder of their lives without recurrence. As reported by the National Cancer Institute's Surveillance, Epidemiology, and End Results program, women diagnosed with early-stage

breast cancer have a 5-year survival rate of 93 percent, in contrast to 70 percent and 17 percent for those diagnosed with regional and distant metastases, respectively. Finally, the clinical course of breast cancer varies greatly among patients, suggesting that there is heterogeneity in the factors that affect both the occurrence and the natural history of the disease.

Breast cancer is now believed to result from a series of alterations (mutations) in the genes of the breast cells. Some such genetic changes may be inherited, but most are not. These alterations can result in an increased likelihood of additional genetic changes (genomic instability), uncontrolled cell growth (proliferation), invasion into adjacent tissues, and spread to other sites in the body (metastases). The causes of these genetic alterations are largely unknown. Ovarian hormones (estrogen and progesterone) clearly play an important role in the development of breast cancer. It appears likely that influences beginning very early in life and continuing throughout adulthood are important. At this time, there are no proven methods of preventing breast cancer.

Some improvements in breast cancer diagnosis and treatment have occurred over the past few decades. A major advance has been achieved through screening with mammography and clinical breast examination. Screening mammography can detect many cancers before they are clinically evident and can lead to a breast cancer mortality reduction of about 25 percent. However, the mortality benefit from mammography has been unequivocally demonstrated only in women aged 50–69. Possibly due to limitations in study design and implementation, the data for women aged 40–49 are inconclusive, and there is a paucity of information regarding the effectiveness of screening women aged 70 and older, despite their high risk.

Breast-conserving treatment (consisting of excision of the cancer—commonly referred to as "lumpectomy" combined with breast irradiation) results in survival rates equivalent to those following mastectomy and provides important quality-of-life gains for many patients. In addition, new surgical techniques facilitate breast reconstruction in patients treated with mastectomy. Drug treatment, such as chemotherapy and Tamoxifen, given at the time of local therapy can decrease breast cancer mortality. While these improvements are important, the survival benefit of about 26 percent is relatively modest given the magnitude of the problem, and is achieved at a substantial cost in toxicity. Most current therapies (surgery, radiation therapy, and chemotherapy) are toxic to normal tissues and organs and thus frequently impact negatively on quality-of-life. Moreover, although the last decade has brought refinements in the available treatment modalities, no major treatment advances have been introduced, and the mortality rate has remained constant.

Even these modest improvements are not uniformly provided for all women. For many women, optimal early detection, diagnosis, and treatment measures are unavailable for financial reasons—they are unable to pay and have inadequate or no health insurance. These women represent a large and growing percentage of the population. Access is a particular problem for women who are low-income, minority, young, old, and living in rural areas. The inequities of this situation have become painfully manifest. Even well-insured women with adequate resources often do not receive the best of care, indicating the presence of significant non-financial barriers to optimal health services delivery.

The past decade has seen a major increase in understanding of the basic biological processes underlying both normal cell division and growth and the biology and genetics of cancer. This knowledge is beginning to be applied to breast cancer. Many excellent investigators have been supported in a broad spectrum of breast cancer research by the National Cancer Institute, the American Cancer Society, and other federal agencies and private organizations. This and other basic biomedical and cancer research have increased our understanding of many aspects of breast cancer and led to some promising new approaches for patients. However, more detailed information is needed about the biology and action of hormones on the normal breast, the genetic changes that lead to breast cancer, biologic factors that cause these genetic changes, and the means by which breast cancer cells grow and spread. It is reasonable to hope that this information will lead to new, more specific methods of earlier detection and diagnosis, treatment, and prevention.

In Fiscal Year 1993, the Department of Defense received an appropriation of $210 million to spend over 2 years on a breast cancer research program. The Commission notes the effort being made by the Army to ensure that this money is well spent, including an Institute of Medicine study commissioned by the Department of Defense to recommend funding priorities. The Institute of Medicine advised that most of the money be spent on investigator-initiated research projects, with some funds allocated to training, recruitment, and infrastructure enhancement.

There is a widespread sense of urgency that more can and should be done to address the problem of breast cancer in this country. This report provides our findings and recommendations. The Commission concludes that more and sustained resources are required to address breast cancer problems effectively. Specific areas and approaches that we believe are most likely to result in meaningful progress are emphasized. Our recommendation for support of breast cancer research at a level of no less than $500 million per year is congruent with the funding level recommended in the Fiscal Year 1995 NCI bypass budget.

Breast Cancer Etiology and Prevention

Findings

- The ultimate goal of breast cancer research is prevention. To develop effective prevention strategies, basic and epidemiologic research must first identify risk factors that can be modified. Prevention studies can then determine the most useful approaches to reducing breast cancer risk by modifying such factors. Prevention trials can evaluate the relative effectiveness of modifying several risk factors and determine the impact of changing single risk factors.

- Today, the most promising areas of research for understanding breast cancer causes and developing optimal prevention methods include: genetics, hormones, diet, physical activity, environmental risk factors, premalignant and tumor markers, and, for secondary prevention, understanding the metastatic process.

Genetics and Tumor Markers

- There is both molecular and epidemiologic evidence that genetic changes are involved in the development of breast cancer, as has been observed for all cancers. Mutations in normal genes, loss of tumor suppressor genes, and altered expression of cellular proto-oncogenes may all be involved in converting a normal breast cell to a malignant one. Additional genetic changes altering expression of proteins on the tumor cell surface can increase or decrease tumor aggressiveness or metastasis. Knowledge of these genes and the proteins they encode potentially may be used to facilitate early detection and diagnosis and to identify high-risk women for prevention trials.

Hormones

- Being a woman is the major risk factor for breast cancer. Women develop breast cancer not only because they have breasts, but also because they have ovaries. Sex hormones, particularly the steroids made by the ovaries, have a central role in breast cancer. They increase the circulating level of two key ovarian hormones—estradiol and progesterone—and modify the levels of other hormones and locally acting growth factors. These changes alter the hormonal environment in the breast, increasing breast cancer risk.

- Other proxy indicators of hormonal activity support the concept that an altered hormonal environment is a major influence on breast cancer risk. Early age at menarche, late age at menopause, obesity in postmenopausal women, nulliparity, and older age at first full-term pregnancy are each associated with increases in risk.

- The effects of steroid hormone contraceptives and hormone replacement therapy have been studied extensively, but the findings have not been totally consistent. However, with each of these hormonal treatments, some elevation in breast cancer risks are noted for specific subgroups of women or in relation to particular characteristics of the hormonal regimen.

Diet

- Five-fold international differences in breast cancer incidence rates and major changes in rates among migrating populations indicate that non-heritable factors play a major role in disease development. Correlations between dietary factors and

breast cancer incidence rates internationally, as well as animal studies, suggest that nutritional factors strongly influence development of breast cancer. At this time, no dietary change has been proven to reduce breast cancer risk in humans.

- Alcohol: A modest positive association between alcohol consumption and breast cancer risk has been shown in many case-control and cohort studies.

- Vitamin A and precursors (carotenoids): Animal studies show reduced mammary carcinogenesis from high doses of vitamin A and related synthetic compounds; human case-control and cohort studies suggest a modest protective effect of preformed vitamin A and carotenoids.

- Total energy intake: In animal models, restricting total energy intake profoundly and consistently reduces mammary carcinogenesis. Human epidemiologic data are consistent with an important effect of childhood and adolescent energy balance (caloric intake and energy expenditure) as rates of breast cancer are associated with height.

- Plant constituents: In several studies, women with higher vegetable intake experienced lower rates of breast cancer. Epidemiologic evidence does not generally support a major role for dietary fiber in breast cancer prevention, although this was suggested in some laboratory studies.

- Dietary fat: In some animal models, high-fat diets increase mammary tumors; polyunsaturated fats appear to have the strongest influence. Some human case-control studies show an association between fat intake and breast cancer risk, but little or no association has been shown in all recent, large, prospective studies, which are less subject to methodologic biases. Protective effects of very low fat intake or alterations in dietary fat early in life cannot be excluded by available data.

- Vitamin D: Women in latitudes with low sunlight exposure, and presumably lower vitamin D levels, appear to have higher breast cancer incidence rates, but more direct evidence for a protective effect of vitamin D is lacking.

- Little is known about the influence of dietary factors on breast cancer prognosis.

Physical Activity

- A few studies have suggested that breast cancer risk is lower among female athletes and among women who have engaged in moderate physical activity.

Environment

- There have been few studies of environmental or occupational exposures as etiologic agents for breast cancer. Most conducted to date were severely flawed methodologically or based on small samples. Research on the effects of exposures to environmental and occupational agents must include assessment of known breast cancer risk factors.

- For none of the 30 known human chemical carcinogens is the human breast the primary site for the initiation of cancer. Exposure to high doses of ionizing radiation, such as that experienced by female atomic bomb survivors in Japan and women who had multiple fluoroscopic examinations for tuberculosis, is known to increase the risk of female breast cancer. Whether non-ionizing radiation from electromagnetic fields increases breast cancer risk is currently being studied.

Recommendations

Etiology

Genetics and Tumor Markers

- Evaluate the role of proto-oncogenes in normal breast tissue growth, differentiation, and reproduction.

- Identify genetic changes during the transformation from normal mammary tissue to premalignant to frankly malignant tissue.

- Evaluate the specific effects of point mutations or deletions of specific oncogenes, tumor suppressor genes, or chromosomal segments associated with breast cancer.

- Identify intermediate or premalignant events or markers of events that occur in the interval from the start of breast abnormalities to the detection of breast cancer. This will lead to earlier diagnosis, higher cure rates, and the development of rational preventive measures.

- Study new marker technologies for the identification of premalignant changes that could be targets for preventive interventions. As such technologies become available, they should be evaluated in multi-investigator or multi-institutional cooperative clinical research groups, which should establish quality control guidelines and design and conduct peer-reviewed clinical trials with adequate power to validate the sensitivity and specificity of new markers and tests.

- Enact federal regulations to limit the widespread sale and clinical use of markers of modifiable premalignant changes (when they become available) that are still experimental, and for which firm quality control guidelines and usefulness have not been established.

Hormones

- Study epithelial cell proliferation and hormonal control of the normal breast during the adolescent and adult menstrual cycle, during pregnancy and lactation, during systemic contraceptive use, and during hormone replacement therapy.

- Identify the genes in the normal breast and in breast cancers that are specifically regulated by endogenous hormones and growth factors, and by hormones in contraceptives and hormone replacement therapy.

- Conduct human research on "low-dose" hormonal contraceptive regimens, and compare the effects of estrogenic versus progestational components of systemic contraceptives on breast tissues.

Diet

- Study basic mechanisms of the preventive role of retinol and carotenoids.

- Define the dose-response relationships and the relative contributions of various forms of dietary vitamin A.

- Elucidate the mechanisms whereby energy restriction reduces mammary carcinogenesis.

- Investigate the relationship between specific types and amounts of dietary fat and protein and breast cancer incidence. Such studies should include a wider range of dietary intakes and examine diets beginning in childhood.

- Expand laboratory, clinical, and epidemiologic research on non-nutritive protective factors in vegetables and fruits, including screening the food supply for potential preventive agents.

- Study mechanisms by which moderate alcohol intake could increase the risk of breast cancer, with one focus being the relationship of alcohol consumption to hormone levels.

- Evaluate the interaction between dietary factors and markers of genetic predisposition as the latter become available.

- Investigate the possible relationship between vitamin D status and breast cancer risk.

- Conduct observational studies and clinical trials on the effect of dietary factors on breast cancer prognosis.

Environment

- Investigate the molecular nature of the carcinogenic process in breast epithelium to understand mechanisms by which environmental chemicals might influence mammary carcinogenesis.

- Conduct animal studies on mechanisms of species differences in susceptibility to chemically induced mammary cancers to increase understanding of human diversity in susceptibility.

- Study occupational exposures to chemical and other carcinogens and breast cancer risk in the context of other known risk factors.

- Investigate exposures to natural and synthetic estrogenic chemicals in the environment and their effects on breast cancer risk, particularly during prenatal, prepubertal, and pubertal periods. Such exposures must be evaluated in the framework of known breast cancer risk factors.

- Develop methodologies needed to study environmental risk factors: molecular markers of exposure and susceptibility, improved methods of assessing dose-response relationships, and mechanisms of enzymatic transformations of precursor molecules to active carcinogens in humans.

- Determine the variable effects of individual and multiple etiologic factors on breast cancer risk by age at exposure.

- Continue studies of Japanese atomic bomb survivors, particularly women exposed *in utero* and during adolescence; evaluate the effects of hormonal, dietary, and genetic factors on susceptibility to breast cancer due to radiation exposure.

Prevention

- Develop approaches to modulate or eliminate the expression of specific oncogene products or abnormal genetic segments in premalignant breast tissue.

- Investigate hormonal chemoprevention intensively through basic, epidemiologic, and clinical studies. Research should focus on the development of pure antiestrogens and antiprogestins, the elucidation of hormonal regimens that mimic the protective effects of early pregnancy, work with retinoids and other vitamins, non-steroidal hormones and hormonal antagonists as systemic contraceptives, and non-hormonal contraceptive methods.

- Conduct observational studies and clinical trials on the effects of modifying multiple risk factors—for example, diet, physical activity, and hormones.

- Complete the Tamoxifen trial to determine whether it can prevent breast cancer among high-risk women.

Screening and Early Detection and the Development of New Technologies for Detection and Diagnosis

Findings

- While prevention is the ultimate goal, earlier detection increases the likelihood of reducing mortality and should have a high research priority.

- Mammography in conjunction with breast physical examination has been shown to reduce mortality from breast cancer in women ages 50–69. Data regarding the benefit from mammography screening in women ages 40–49 are inconclusive, possibly due to limitations in study design or implementation.

- The technology of film-screen mammography has improved greatly over the past decade, but its sensitivity and specificity are still not adequate to detect all breast cancers at an early stage, especially in premenopausal women.

- Screening mammography is underutilized, especially by women aged 60 and older, who are most at risk. Racial and ethnic minorities and low-income women are also less likely to get mammograms.

- Failure of health care providers to recommend mammography is a major cause of poor utilization.

- The Mammography Quality Standards Act, designed to ensure high-quality mammography facilities across the country, was passed in 1992, but has not yet been implemented. The Food and Drug Administration is responsible for implementing this law, but instead is expending its efforts modifying it.

- Ultrasonography has limited use for breast cancer detection. Newer imaging modalities such as positron emission tomography and magnetic resonance imaging are still under development and should be used only in the context of well-designed studies.

Recommendations

Practice and Outreach

- Immediately implement the Mammography Quality Standards Act to ensure that all women receive mammography of acceptable quality, and remove overlapping and conflicting standards. Current multiple certifications required at federal and state levels and from private organizations impose an excessive burden on mammography facilities, waste tax dollars, and increase costs.

- Promote utilization of screening mammography and clinical breast examination for groups of women who are currently being screened at disproportionately low rates (e.g., older women, rural women, women of lower socioeconomic status, and specific racial and ethnic populations, especially African American, Native American, Latino, and Asian women). This will require gathering additional information on barriers to screening and the information needs of these groups, and using existing information to develop effective educational materials and programs. Special attention should be given to conveying the message that increasing age is the major risk factor for developing breast cancer. These efforts should recognize the diversity of needs among and within specific groups and the necessity to develop materials, services, and interventions that address these specific needs.

- Educate and encourage physicians to recommend screening mammography actively.

- Provide screening and appropriate follow-up services for women, regardless of financial status or extent of insurance coverage.

- Help women assure their own breast health by providing financial and psychological support, enabling them to take responsibility for following recommended breast cancer screening guidelines and practicing breast self-examination.

Screening Research

- Conduct further studies to determine the mortality benefit of screening in women ages 40–49 and in women ages 70 and older, the optimal periodicity of screening in relation to age, and the relative utility of mammography and clinical breast examination. Investigators should first assess whether case-control studies could answer some of these questions as a less costly and more rapid approach than randomized controlled trials. Such studies should use state-of-the-art mammography and must be well designed and well executed. Consideration should be given to providing support for the ongoing trial in the United Kingdom to resolve questions related to screening women in their 40s.

- Develop a system designed to provide information about the practice of breast cancer screening in the United States.

- Assess the effects of co-morbid medical illnesses on breast cancer screening outcomes in women in different age groups.

- Determine the full range of breast cancer screening roles that nurses and physician extenders can play.

New Technologies Research

- Develop better technologies for detection and diagnosis. Such technology should detect breast cancer at its earliest stages, be highly sensitive and specific, non-invasive, and effective for women of all ages.

- Study the feasibility of earlier detection using computer-assisted mammography interpretation and techniques using digitization of mammographic images. Continue research into improving ultrasonography.

- Determine the comparative efficacy of stereotactic fine-needle and core biopsy and ultrasound-guided fine-needle and core biopsy with the goal of reducing the need for excisional biopsy.

Improving the Outcome for Breast Cancer Patients: Treatment and Quality-of-Life Effects

Findings

- Despite some recent improvements in treatment, many thousands of women diagnosed with breast cancer die of the disease. No currently available treatment can be defined as curative.

- Since current treatments result in modest improvements in survival, assessing the effects of treatment on quality of life is important to inform patients adequately about treatment options. Quality-of-life issues include functional status, psychological well-being, social (work and home) functioning, sexuality and fertility, and spiritual well-being. Quality of life is influenced by personal factors (e.g., developmental stage and social support), clinical factors (e.g., stage of disease and type of treatment), and demographic factors (e.g., ethnicity and geographic location). The effects of treatment on long-term quality of life are not adequately known at this time.

- Adjustment to breast cancer is an ongoing process. While some patients do well following diagnosis and treatment, many experience adjustment difficulties in succeeding years. Fear is an overriding issue for women who have had a diagnosis of breast cancer.

- Treatment recommendations are best made in a clinical setting that includes experts in the various disciplines. Patients should be empowered to participate actively in making treatment decisions.

Recommendations

Treatment

- Exploit advances in molecular biology to find a cure for breast cancer. In particular, new and more specific therapeutic strategies should be developed, including: therapy directed at tumor growth factors or growth factor receptors; inhibitors of angiogenesis and metastases; gene therapy; and immunologic therapy, including vaccines. Innovative research should be encouraged.

- Identify cell surface factors associated with the ability of tumors to invade and metastasize; develop strategies to modulate the expression of such factors. Explain the predilection of metastatic cells to home to some but not other target organs.

- Improve current treatment strategies to make them more effective—identify mechanisms of resistance to hormonal and chemotherapy, develop ways to avoid or overcome resistance, evaluate dose intensification of chemotherapy in primary and metastatic breast cancer, evaluate pre-operative chemotherapy effectiveness, and optimize the long-term results of breast-conserving treatment and breast reconstructive surgery.

- Determine prognostic and predictive factors (or markers) for systemic therapy in order to select patients who are likely to benefit. However, it is necessary to regulate the clinical use of breast cancer markers that are still experimental. Markers should be made available outside the confines of a clinical trial only

when they have been adequately validated and when firm quality control guidelines for their use have been established.

- Continue drug development research to discover new, more active agents.

- Ensure adequate funding for clinical investigations of new treatments and provide positive inducements for physicians and patients to participate in studies of promising new approaches. In particular, continue support of single institution pilot studies and of cooperative group randomized clinical trials.

- Define the natural history of ductal carcinoma *in situ* and other proliferative breast lesions, including factors strongly associated with progression to invasive breast cancer.

Quality-of-Life

- Evaluate the frequency, severity, and persistence of adverse physical changes caused by treatment and develop strategies to deal with these changes. In particular, evaluate treatment effects on fertility in premenopausal patients, and on sexual function in women of all ages. Strategies to treat menopausal symptoms and arm edema, as well as improved breast implants or other methods of reconstruction, must be developed.

- Include quality-of-life measures in clinical trials of new treatment and prevention regimens and approaches.

- Develop guidelines for psychosocial evaluation and support over time of women diagnosed with breast cancer and those at risk for the disease; develop and test effective interventions to improve psychosocial adjustment. Specifically, studies should involve patients of all ages, women at high risk for developing breast cancer, and patients with recurrent disease. Research also should include the effects of diagnosis and treatment on patients' families and social functioning.

- Develop better strategies for supportive care of end-stage breast cancer patients and ensure availability of these services to patients and their families.

- Conduct clinical trials to provide information on the effects on survival and quality of survival of systemic hormonal contraceptives, pregnancy, and hormone replacement therapy at menopause in breast cancer survivors, including women in whom treatment of premenopausal breast cancer induced premature menopause.

Infrastructure, Education, and Training

Findings

- Breast cancer research requires resources such as repositories, registries, and specialized research centers which must operate for many years. It is difficult to obtain stable, long-term funding to establish and maintain such resources outside an hypothesis-driven research proposal.

- Advances in understanding the biology and genetics of breast cancer are not likely to be immediately applicable to improved prevention and treatment methods. A new generation of trained, basic, translational and clinical investigators is needed to ensure that the knowledge gained from basic research leads to human benefit, specifically the prevention and cure of breast cancer.

- It is essential to ensure that clinical studies of prevention, detection, diagnosis, and treatment include women of diverse ethnic and sociocultural backgrounds. Culturally acceptable study design and recruitment of women from varied ethnic and racial groups are facilitated by the participation of investigators sensitive to sociocultural issues and who also come from diverse backgrounds.

Recommendations

- The preponderance of research funding should be directed to investigator-initiated inquiry. A major emphasis should be placed on supporting innovative and imaginative research.

- Expand or create specialized research resources: breast cancer SPOREs (Specialized Programs of Research Excellence), the National Cancer Institute's Surveillance, Epidemiology, and End Results program, and other high-quality cancer registries capable of providing data to monitor long-term trends in breast cancer, relevant animal models and cell lines, and repositories for biological specimens.

- Develop an information-sharing network for breast cancer researchers.

- Fund training grants specifically targeted to the next generation of investigators in all aspects of breast cancer research.

- Train investigators in translational research and in clinical trials to facilitate the development of improved prevention, detection, and treatment strategies.

- Emphasize during research training the role of ethnic and sociocultural diversity in risk of breast cancer, as well as the need to develop acceptable and sensitive strategies for research on prevention, early detection, diagnosis, and treatment for diverse population groups.

- Train future clinical investigators in both translational and clinical trials research. These investigators need broad training in the biology, genetics, and clinical manifestations of breast cancer, and in epidemiology and biostatistics.

- Utilize tumor boards in institutions that treat breast cancer to ensure optimal care through proper and timely input from various cancer specialists and to help train young physicians.

- Ensure that oncologists (medical, surgical, radiation, and nursing) receive interdisciplinary training to improve the quality of breast cancer care.

- Train clinicians of diverse ethnic heritage in breast cancer care.

- Promote continuing education programs for all professional and technical personnel dealing with breast cancer patients to ensure that advances in care are translated to practice.

- Ensure that medical school, residency, and fellowship training programs and training for advanced nursing practice include education on the need for regular breast examinations, including mammography and clinical breast examination, and on the performance of a thorough clinical examination of the breast.

- Encourage health care providers to educate patients about breast cancer, including treatment and rehabilitation options.

Public Communication

Findings

- Information appropriate for and appealing to the mass media and information necessary for public education differs substantially. A fundamental principle of communicating with the public about breast cancer issues is to distinguish between information that is newsworthy and that which is needed for educational purposes. News media professionals generally consider it their responsibility to report news accurately, but not to serve as public educators. Therefore, channels other than the media are required for education.

- There is a discrepancy between the media attention given to breast cancer and its importance as a public health problem. While the media do give some attention to breast cancer, more resources could be expended by the media to present breast cancer-related issues to the public. For example, newspapers, television stations, and radio stations send reporters to international conferences on AIDS, but are very unlikely to send anyone to scientific meetings concerned with breast cancer. To some extent, this discrepancy is attributable to advocacy groups. It is clear that news media respond to activism. The more assertive breast cancer advocacy groups are, the more attention breast cancer will receive from the press.

- A significant segment of the U.S. population has a low level of literacy. It is essential to present educational materials and media messages in diverse formats so that all target audiences are reached. In some situations, it may be best to present both news and education via audio and visual channels (radio and television).

Recommendations

- Support a national work group on low literacy and cancer information and education.

- Make publicly funded public information and educational materials understandable to individuals at all literacy levels.

- Encourage breast cancer scientists, clinicians, and advocates to collaborate to determine the most effective methods for presenting clear messages to the public which neither understate nor overstate specific issues or overall progress in breast cancer research and care.

- Emphasize coordination of public information efforts between components of the National Institutes of Health and with other federal agencies, such as the Centers for Disease Control and Prevention.

- Work with news media to promote accurate, responsible, and adequate coverage of breast cancer issues.

Patient Advocacy

Findings

- Breast cancer is a public health problem involving multiple constituencies. It must be a high priority for all concerned with the health of women. Improving breast cancer research, prevention, detection, and treatment is a shared responsibility of consumers, health care providers, biotechnology and pharmaceutical industries, health educators and researchers, public health agencies, legislators, third-party payors, the National Cancer Institute, and other government agencies.

- Over the past decade, patients and their families have promoted breast cancer as a national priority and have focused attention on the need for a cure and for prevention.

- Service, patient support, and advocacy organizations exist for women, including underserved and minority women, at local, state, regional, and national levels. These organizations are valuable resources for many women and are influential in shaping public policy. Voluntary organizations fund and operate breast cancer screening programs, often targeted to underserved and minority women, and provide outreach and support to women during and following treatment for breast cancer. Some fund breast cancer research. Patient organizations provide psychosocial support; advocate for individual patients within the health care system and with payors; urge specific research emphases; and work at local, state, and national levels for policies and legislation on many breast cancer issues. Unfortunately, many minority and low-income women do not feel that most existing organizations represent them, although there are some exceptions. Improved communication between patient advocacy groups and voluntary and government organizations would be beneficial to all.

- Breast cancer advocates want more participation in decision-making concerned with research and the optimal use of breast cancer research funding.

Recommendations

- Encourage patient advocates and voluntary organizations to work cooperatively to achieve legislation that provides funding, research, treatment, education, and support for women with breast cancer.

- Support voluntary and advocacy organizations' work to ensure access to care for all women and fund community-based programs to bring breast cancer information, education, and interventions to affected groups where they live and work.

- Ensure that health care reform implementation in each state reflects breast cancer issues specific to that population and geographic area.

- Educate physicians about the medical and psychosocial aspects of breast cancer and women's needs for screening, diagnosis, treatment, and continuing care. Physicians must include the woman as a partner in arriving at a diagnosis and choosing the most suitable care.

- Integrate breast cancer advocates into decision-making regarding the optimal use of breast cancer research funding.

- Encourage efforts by patient advocate organizations and other voluntary and educational groups to ensure that women are fully informed and educated about their own breast health, including adopting healthy lifestyles, practicing monthly breast self-examination, following recommended guidelines for early detection, and obtaining immediate diagnostic and treatment services when an abnormality is observed.

Public Policy

Findings

National and State Legislation

- Recent breast cancer research funding increases have provided a large infusion of support for this area of biomedical investigation and raised the priority level of breast cancer within biomedical research. However, increased National Cancer Institute support for research on breast and other specific cancers without the addition of sufficient funds has required redirection of resources from other areas of cancer research. A sustained level of increased funding should include additions to the budget to strengthen breast cancer research specifically, and cancer research generally.

- In addition to federal legislation pertaining to aspects of breast cancer detection and treatment, states have enacted laws to provide quality assurance for mammography, ensure that treatment options are presented to women diagnosed with breast cancer, mandate payment for some off-label uses of chemotherapeutic drugs, and improve access to mammography by requiring insurance companies and Medicaid programs to cover breast cancer screening.

- Impending health care reform is projected to improve access to breast cancer screening, education, treatment, and supportive care. The main principles expected to govern these reforms include security in health care coverage, eliminating exclusions for pre-existing conditions; provider of quality of care and accountability; cost controls; and comprehensiveness of care.

Payment Policies

- Payment policy for all aspects of breast cancer care has a major health, psychosocial, and economic impact on women. Current problems in payment for breast cancer care include inadequate insurance coverage of screening mammography and breast clinical exam; no reimbursement for preventive interventions; limited or no payment for routine care associated with clinical trials; no reimbursement for drugs that have been approved by the Food and Drug Administration for cancers other than breast cancer, but not for breast cancer (off-label use); lack of reimbursement for physical and psychological rehabilitative services; lack of coverage for prostheses, wigs, transportation, or other indirect treatment or rehabilitation costs; and no reimbursement for reconstructive surgery following mastectomy.

- The ability to purchase health insurance, enroll in a group policy, or obtain publicly funded care is critical for access to care. Exclusion of pre-existing conditions leaves women previously diagnosed with breast cancer without coverage in the event of a recurrence. Women who have been diagnosed with breast cancer cannot change jobs because future treatment for breast cancer would be excluded from coverage. Women with no coverage or inadequate insurance often experience delays in diagnosis and treatment.

- Affordability of care and of health insurance is an important issue. In small companies, breast cancer patients may be discriminated against and feel guilty if the costs of their care lead to a large insurance premium increase for their co-

workers. Increased premiums and patients' out-of-pocket costs for breast cancer care can affect family resources and cause the breast cancer survivor to feel guilty.

- There is a very specific problem with regard to reimbursement for mammography. While the current guidelines of the National Cancer Institute, the American Cancer Society, and other professional organizations recommend annual mammograms for women 50 and older, Medicare provides reimbursement every other year for women 65 and older and does not provide any coverage for breast clinical examination.

Recommendations

National Legislation

- New funds should be appropriated to support the President's Cancer Panel Special Commission on Breast Cancer's recommended program at a level no less than $500 million per year until breast cancer prevention and cure are achieved. This research effort should be under the leadership of the National Cancer Institute.

State Legislation

- Support state legislation to provide quality assurance for mammography and insurance coverage for screening, diagnostic tests, treatment, and patient care costs of clinical trials.

Payment Policies

- Decisions about health care coverage in this country should involve all members of our society and take into consideration the society as a whole, government responsibilities, and the concerns of business.

- Increase access to affordable health care coverage by:

  - eliminating pre-existing condition clauses;

  - providing a universal health care package regardless of financial status or job or career changes; and

  - utilizing and adequately reimbursing primary care physicians and other providers such as nurse-practitioners and physician assistants.

- Provide comprehensive coverage for reasonable costs of screening and diagnostic tests, treatment, rehabilitation, and psychosocial services by:

  - consensus development of practice guidelines; and

  - covering treatment known to be effective and listed in the three compendia (*AMA Drug Evaluations, United States Pharmacopeia, Hospital Formulary*) whether or not FDA-approved specifically for breast cancer.

- Encourage and support breast cancer clinical research by:

  - providing coverage of standard health care costs incurred in peer-reviewed clinical trials;

  - providing coverage of interventions not yet proven to have medical benefit only in the peer-reviewed clinical trial setting; and

  - providing incentives to industry and the private sector to support treatment costs of clinical trials.

Special Issues for Minority and Underserved Women

Findings

- Minority and underserved women are heterogeneous, encompassing diverse ethnic groups (e.g., Native Americans, African Americans, Latinas, and Asian Americans); rural women; women with low literacy; women with inadequate health care, health insurance, or financial resources; women with disabilities from other illnesses or injuries; and women 65 and older, who often do not receive breast cancer screening or obtain state-of-the-art treatment.

- Diversity must be a key word in breast cancer research, prevention, diagnosis, treatment, and supportive and continuing care. No subgroup of women is homogenous: white women in the United States are considered as a single, homogeneous entity, yet they have diverse demographic, socioeconomic, and ethnic backgrounds which influence their risk of breast cancer and their potential for access to the full range of appropriate care from prevention and early detection to rehabilitation. Similarly, other ethnic groups, such as Latino, African American, and Asian women are treated as if they all were similar. Diversity within these groups in culture, tradition, language, education, and other factors associated with breast cancer risk and access to optimal care must be considered in developing culturally sensitive programs.

- Access to breast cancer education, early detection, treatment, and rehabilitation is often restricted among women having one or more of the characteristics described above. Breast cancer research rarely includes women from many of these populations and fails to encompass their issues in developing strategies for optimal care.

Recommendations

- Where scientifically appropriate, structure clinical trials to reflect the racial and ethnic population diversity.

- Build partnerships with underserved communities to encourage their involvement and self-advocacy in health care. Hospitals, clinics, health departments, and other providers should be encouraged to assist the underserved in navigating the health care system. Such strategies will increase early detection and reduce costly use of emergency rooms.

- Precede design of outreach and research projects in minority populations with consultation and interaction with community leaders where the project will take place. Provide adequate funding for long-term efforts.

- Conduct behavioral/social research on culturally sensitive approaches to current and future primary prevention strategies and ways to increase access to and utilization of early detection techniques and state-of-the-art treatment.

- Reduce geographic barriers to optimal education, early detection, treatment, and rehabilitation, particularly in rural areas.

- Investigate the psychosocial impact of breast cancer on women and their families and differences related to diversity by ethnicity, urban/suburban/rural residence, and socioeconomic status.

- Conduct studies to determine risk factor prevalence across diverse ethnic, socioeconomic, and cultural (e.g., urban/suburban/rural) populations.

- Make available breast cancer incidence and mortality data for all major ethnic groups: African American, Latino, Native American, Chinese, Japanese, Native Hawaiian, etc. The U.S. Census Bureau should provide intercensal population estimates for these groups. The National Cancer Institute's Surveillance, Epidemiology, and End Results program should provide the incidence data, while the mortality information should be provided by the National Center for Health Statistics.

- Target public information and media channels for providing breast cancer education to specific ethnic communities by: focusing on their media outlets, emphasizing radio advertisements and print media, and developing diverse programming that takes into account differences within an ethnic group in acculturation, literacy, language, and traditional cultural practices and beliefs.

- Remove linguistic and cultural barriers to screening, treatment, and rehabilitation.

APPENDIX A: PRESIDENT'S CANCER PANEL SPECIAL COMMISSION ON BREAST CANCER MEMBERSHIP ROSTER

Chairman
Nancy G. Brinker
Founding Chairman
Susan G. Komen Breast Cancer Foundation
Dallas, Texas

Dorit D. Adler, M.D., M.P.H.
Associate Professor of Radiology
Associate Director
Division of Breast Imaging
University of Michigan Medical Center

Karen H. Antman, M.D.
Chief, Division of Medical Oncology
Columbia Presbyterian Medical Center
New York, New York

Zora K. Brown
Founder and Chairman
Cancer Awareness Program Services
Washington, D.C.

Pelayo Correa, M.D.
Professor of Pathology
Louisiana State University Medical Center

Gerald D. Dodd, M.D.
Radiologist and Professor of Radiology
The University of Texas M.D. Anderson
Cancer Center

Karen Hassey Dow, R.N., Ph.D.
Nurse Researcher
Beth Israel Hospital
Cambridge, Massachusetts

Harmon J. Eyre, M.D.
Deputy Exec. V.P. for Medical Affairs and
Research
American Cancer Society
Atlanta, Georgia

Jay R. Harris, M.D.
Clinical and Educational Director
Professor in Radiation Oncology
Shields Warren Radiation Laboratory
Joint Center for Radiation Therapy
Harvard Medical School

Kathryn B. Horwitz, Ph.D.
Professor of Medicine and Pathology
University of Colorado
Health Sciences Center

Barbara S. Hulka, M.D., M.P.H.
Kenan Professor and Chair
Department of Epidemiology
School of Public Health
University of North Carolina

Mary-Claire King, Ph.D.
Professor of Epidemiology
School of Public Health
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Sherry L. Lansing
Chairman and CEO
Paramount Motion Picture Group
Los Angeles, California

Sam Shapiro
Professor Emeritus
Health Services Research and
Development Center
School of Hygiene and Public Health
The Johns Hopkins University

S. Eva Singletary, M.D.
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G. Marie Swanson, Ph.D., M.P.H.
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Director, Cancer Center
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Reed V. Tuckson, M.D.
President
Charles R. Drew University of Medicine
and Science
Los Angeles, California

Frances M. Visco, Esq.
President
National Breast Cancer Coalition
Philadelphia, Pennsylvania

Walter C. Willett, M.D., M.P.H., Dr.P.H.
Nutrition Department
Harvard School of Public Health

Executive Secretary
Iris J. Schneider
Assistant Director for Program Operations
and Planning
National Cancer Institute

Appendix B: Meetings of the President's Cancer Panel Special Commission on Breast Cancer

May 28, 1992
Overview of Breast Cancer Research

July 8, 1992
Issues in Basic Research

September 23, 1992
Radiation and Toxic Exposures as Risk Factors

Dietary Influences on Risk and Implications for Prevention

October 23, 1992
Patient Advocacy and Voluntary Organizations

November 12, 1992
Hormonal Factors

January 11-12 1993
Treatment, Rehabilitation, and Quality of Life

February 23, 1993
New Product Development for Breast Cancer Prevention, Treatment, Detection, and Diagnosis

March 18-19, 1993
Screening and Early Detection

Development of New Technologies for Detection and Diagnosis

April 29, 1993
Possible Environmental Influences on Breast Cancer

Health Care Delivery and the Role of the Payors

June 25, 1993
Information Dissemination and the Role of the Media

July 21, 1993
Public Policy and Legislation

Copies of meeting agendas, transcripts, and meeting summaries available by writing to:

President's Cancer Panel Special Commission on Breast Cancer
Attention: Nora Winfrey
National Cancer Institute
Building 31, Room 4A34
Bethesda, MD 20892

APPENDIX C: PRESIDENT'S CANCER PANEL MEMBERS

Harold P. Freeman, M.D.
Chairman
Director of Surgery
Harlem Hospital Center
1991 to 1994

Henry C. Pitot, M.D., Ph.D.
Professor of Oncology and Pathology
McArdle Laboratory
University of Wisconsin
1992 to 1995

Nancy G. Brinker
Founder
Susan G. Komen Breast Cancer
Foundation
1992 to 1993

Frances M. Visco, Esq.
President
National Breast Cancer Coalition
1993 to 1996