

Evolution of Federal Support of Chemotherapy Research

Ladies and gentlemen, it gives me great pleasure to be here with you tonight. To the casual observer, my presence as your dinner speaker might suggest that the Rhode Island Section of the American Chemical Society, ~~inviting me to speak here this evening,~~ has bargained for some old-fashioned political oratory perhaps as a change of pace from the scientific presentations which have occupied your afternoon!

However, those of you who know of my principal interests and activities -- both as a Representative to Congress from the Second District of Rhode Island, and as Chairman of the Subcommittee in the House of Representatives having responsibility for Federal appropriations for the Nation's health programs -- are well aware that my interests find a common meeting ground with those of the American Chemical Society in the field of medical research including, among many other areas, that aspect of medical research related to the discovery and development of new and improved means for the treatment of diseases and disabilities with chemicals.

I have experienced considerable personal satisfaction in having a part in the formulation of our national program for conduct and support of scientific research in the past 15 plus years. In these years, there has been dramatic progress in the acquisition of new knowledge both in your field and in its application in medicine.

Chemistry and medicine have served as a common source for countless successful attacks on diseases and disabling conditions that have plagued man for centuries. I am indeed sorry that I was unable to attend your sessions earlier today when two programs were discussed that epitomize the increasing rôle of chemistry as an essential component of the medical sciences.

These two subjects which you discussed -- chemotherapy of cancer and chemotherapy of mental disease -- are reminders, too, of the growing participation by the Federal government in the conduct and support of medical research. It is to the credit of all segments of these national programs that even though we have seen revolutionary accomplishments in the whole field, the growing participation of the Federal government has been evolutionary, not revolutionary.

So that we may gain some perspective on this expanding Federal rôle, with perhaps some sense of its movement and direction, I would like to trace for you very briefly some of the patterns that have been developing during my years of participation in Federal health legislation.

If I may be permitted an over-simplification, one way to view the Nation's medical research effort may be by placing it on a scale, if you will, with support on one side and accomplishments or results on the other. As a Nation, we would be satisfied -- perhaps pleased -- if the scale remained perfectly balanced. In considering the support of and the results from medical research, one is reminded of the age-old question about the chicken and egg -- Which came first?

It is true that the dramatic accomplishments of World War II stimulated unprecedented levels of support in the years immediately following, but it must be remembered that those war-born accomplishments were also the products of increased support.

At the close of World War II, the country had its choice. Either we would return to the pre-war levels of effort in medical research, or we would seek to capitalize on the opportunity to support man's effort to extend his horizons in the life sciences. The question was resolved, as are all important questions in our society, by consensus. To most people, whether scientists or laymen, the course seemed clear: If a Nation's scientific effort could produce so well under the stress of war, surely it could flourish to provide an opportunity for better health in peace.

As a result, Congress began to increase appropriations for Federal funds used by the Government to stimulate medical research in private laboratories throughout the country -- in universities and medical schools, in hospital laboratories, and in other research centers. Appropriations also were steadily increased for the operation in Bethesda, Maryland, of what is today one of the world's largest medical research centers -- the National Institutes of Health of the U. S. Public Health ~~Service~~. This is the research program in which I have been most deeply interested; my committee has had responsibility for its appropriations, which have become a significant part of the Nation's total investment in medical research.

The appropriations for NIH, including its own operations and grants for research projects and awards for fellowships and training, amounted to

less than \$3.5 million in Fiscal Year 1946. For 1958, our current fiscal year, their appropriation stands at \$241. million. Lest you conceive of this expansion as a reckless, hell-for-leather throwaway of Federal funds in an effort to BUY new knowledge, let me detail some of its elements.

First, in research project grants: In 1945, this appropriation totaled \$55,000; this year, the same appropriation is a little over \$99 million --- supporting nearly 7000 research projects in virtually every nonprofit research center in the country. Let me assure you now that prior to each year's increase, from 1946 through 1957, the Congress received convincing evidence of (1) the accomplishments and potentialities of existing research projects, and (2) the existence of promising ideas for new and needed research projects.

At the same time, it was necessary for those of us dealing with this program to keep well-informed on two more elements of medical research, namely, the existence of trained manpower to do the research and of adequately equipped facilities in which to carry out the research. To keep these three all-important elements of medical research in relative balance has been no easy task.

The level of support for research training, including fellowships, began to make solid advances in 1947. In that year the appropriation for fellowships and training grants totaled \$428,000 compared to \$57,000 in 1945. But as each year passed and as it became more and more evident that scientific manpower was the most important single factor limiting further progress in the life sciences, the program expanded until today the annual appropriation stands at about \$40 million.

The third element of the Public Health Service's pattern for research support -- research facilities -- received only emergency attention during 1949 and 1950 for heart and cancer research facilities, totalling some \$22 million. More recently, again responding to an evident need for nationwide expansion of health research facilities and equipment, the Congress passed legislation authorizing \$90 million to be made available over a period of three years for construction and equipment of research facilities in all of the health fields. Now finishing its second year, the \$60 million available has been awarded to 150 nonprofit institutions in 38 States. ^{Through matching funds,} This initial investment of \$60 million in Federal money will result in the construction of facilities having a value of over \$390 million.

So much for the expansion of Federal support for medical research. It is a fair assumption, I think, that it has played an important part in the progress that has taken place in the last decade -- progress to which your own field, chemistry, applied in biological studies, has contributed so much.

You know better than I, perhaps, what these accomplishments have been. You may see them primarily as scientific achievements. I may see them, perhaps, more in the light of their meaning to the public as a whole. I am thinking, for example, of the discovery and development of synthetic hormones and related agents for rheumatic disease the widespread availability of penicillin and the development of other antibiotics the development of chemical agents for control of high blood pressure the discovery of chemical agents in the study and treatment of mental illnesses the improved protection against rheumatic fever and valvular heart disease.

the new tests for detection of cancer surgery of the heart the discovery and application of a new vaccine for poliomyelitis the use of radioactive isotopes for studies of body chemistry the development of drugs and chemical agents for treatment of tuberculosis.

As a Congressman, I hear a great deal of discussion of new and better chemical agents, new drugs, new treatments, and even the claim that 50 percent of today's prescriptions could not have been written ten years ago simply because the materials incorporated in them did not exist. But the acid test of progress against disease lies in statistics which show that progress in broad terms.

Perhaps the best single index of health progress is a comparison of over-all death rates. I am told that the decline in death rates since World War II from some of the major illnesses dramatically shows how over a million lives have been saved by modern medicine.

Influenza, for example, has been reduced over 90 percent in its death rate. Once-great killers like acute rheumatic fever, tuberculosis, diseases that cause maternal deaths, and appendicitis have all had the rate at which they cause death reduced over 70 percent. The death rate from syphilis has been brought down over 60 percent; pneumonia, over 40 percent; some kidney disorders, 60 percent; infant death rates, over 30 percent; and paralytic polio, the disease ^{about which much} ~~whose mode of transmission~~ is still unknown, has been reduced dramatically in the past two years. Even high blood pressure, one of the greatest medical problems in terms of the numbers afflicted, has seen some decline in death rates in the past few years.

Most of these tremendous advances, of course, have been made against the so-called infectious diseases. Though the importance of these accomplishments cannot be denied, we must not assume that they lessen the importance of continued research effort. Instead, they are forceful reminders that our population is surviving the rigors and hazards of infancy and infectious diseases only to face the rising incidence of chronic diseases. Long-term mental patients continue to occupy the majority of hospital beds in this country; cancers of all kinds continue to kill a quarter of a million of our citizens every year. The course of action, therefore, has been the rather obvious one -- that of adapting the methods, procedures, and approaches that have been successful in the past to the problems of today and tomorrow.

In this period of rapid growth and accomplishment, many of the most dramatic findings have been the product of the chemical approach to problems of science and medicine. Biochemistry has taken shape, grown, and flourished -- contributing immeasurably to the better health of our people and of people everywhere. In this dynamic age of the role of chemical agents in medicine, the search for and the trial and application of new compounds or groups of compounds have taken varied forms and varied approaches.

I seem to recall that Ehrlich, the discoverer of the first successful medicine for syphilis, called his remedy "606" because it eliminated 605 unsuccessful attempts to find the right formula. This was one of the first empirical, trial-and-error, process-of-elimination programs to be successful. Later, a similar but much broader program aimed at producing malarial suppressants and cures saw the screening of over 15,000 compounds. It is to the lasting credit of medical science that primaquine, one of the three satisfactory compounds

derived from this program, could cure Vivax malaria in servicemen returning from the Korean war at a cost of less than 14 cents per man.

It was against a background of some success in these fields through the "empirical approach" that Congress some years ago became interested in supporting such a program, seeking to explore the possibility that chemotherapy might hold at least one of the answers to the problem of cancer.

In 1953, the Congress asked the National Cancer Institute to explore the feasibility of an engineered, directed research program in the chemotherapy of acute leukemia. A study growing out of that request suggested that fundamental research could best be done in the traditional atmosphere of independent research, but at the same time recognized the need for collaborative studies in certain areas.

Later that year, the National Cancer Institute -- in a first step toward adopting a program philosophy of voluntary cooperation -- awarded a series of research grants to research institutes and medical schools to establish or expand integrated cancer chemotherapy research programs. These grants amounted to almost one million dollars.

Based on the promise in this initial effort, it was decided in July of 1954 that there should be some form of inter-^{organizational}~~institutional~~ cooperation in order for the program to move ahead. In the fiscal year that followed, several actions were taken to expand and integrate the program:

- ... A new advisory committee -- the Cancer Chemotherapy Committee of the National Advisory Cancer Council -- was formed,
- ... The American Cancer Society and the Damon Runyon Memorial Fund

for Cancer Research joined the National Cancer Institute as co-sponsors,

- ... Funds for support of cancer chemotherapy research through grants were increased to \$3 million,
- ... The group of sponsoring agencies was increased to include the Atomic Energy Commission, the Veterans Administration, and the Food and Drug Administration,
- ... A contract program for the support of research and services was instituted, and
- ... The Cancer Chemotherapy National Service Center was established as the staff organization responsible for the program. Since the major support for the program would be through the National Cancer Institute, the Service Center was made part of the Institute at Bethesda, Maryland.

Five advisory panels -- one for chemistry, one for screening, one for pharmacology and biochemistry, one for clinical studies, and one for endocrinology -- were established to assess the state of knowledge in their particular field, to find promising avenues of approach, and to advise on technical aspects of the national program. For the fiscal year beginning in July 1955, the Congressional appropriation was increased to \$5 million. Thus was the skeleton constructed for this program aimed at rapid and comprehensive exploration of all promising leads in the use of chemical substances to treat cancer.

The program has been expanded to the point where it is now being supported to the extent of about \$25 million in Federal funds after less than three years' operation.

You ladies and gentlemen know better than I that the heart of any empirical drug-development program is screening. Perhaps the most significant aspect of the program's early development was that many of the pharmaceutical companies became actively interested in the program, submitted materials for screening, and began to develop cancer chemotherapy programs of their own. Each year now, some 45,000 synthetic chemicals, antibiotic "beers," steroids, and plant extracts are being tested for anti-tumor activity.

Although the chemical control of cancer has not been achieved -- and, indeed, may never be achieved -- great progress within a relatively short period of intensive research indicates that this field is promising. Just 10 years ago, less than 5 percent of children with acute leukemia lived as long as a year. Today, that one-year survival rate has been raised 50 percent by the use of chemicals and adjunct therapy. It is facts such as these that underlie the promise in cancer chemotherapy.

Now I would like to say something about another research program in chemotherapy -- that for mental disease. At first I thought I would like to compare these two programs because both have evolved from an increasing public interest in the potentials of chemotherapy, both have had the support of Congress, and both have been established for administration at the National Institutes of Health. Beyond these common points, however, these programs have widely divergent characteristics, so that my remarks will reflect instead a superficial view of the contrasts inherent in each of the two efforts.

First and most obvious -- though it does not have significant effect on the nature or direction of either program -- cancer kills men; mental illness kills manpower.

Second, in cancer, scientists are still looking for compound, anti-metabolite, antibiotic, or steroid of choice; in mental illness, there is already in being a whole host of tranquilizers and other psychopharmacologic agents that have proved useful in therapy.

A third point is suggested by the second (and this is age-old): New discoveries, while adding to man's store of knowledge, usually have a way of dramatizing how little we know, thus raising new questions to be answered by a national research program focused on the tranquilizing drugs:

Will the drugs lead us to the basic source of the patient's difficulty?

How lasting are the effects of the drugs?

Are they habit-forming, either physically or psychologically?

Can toxicity be reduced or eliminated?

Might widespread use of these drugs be responsible for industrial and motor vehicle accidents?

Will these drugs affect the learning abilities of children under treatment?

These are just a few of the questions that face research scientists in Government, industry, and in private institutions. These questions also have very serious implications for those of us in Congress who have a responsibility for the levels and general direction of research programs in the health field.

Two years ago, a National Conference on the Evaluation of Pharmacotherapy in Mental Illness, sponsored by the National Institute of Mental Health, American Psychiatric Association, and the National Research Council, set up research guidelines based on the experience and judgment of experienced clinicians and researchers. Congress then encouraged the expansion of research in the field by providing \$1.5 million for research grants and conducted research in the laboratories of the National Institute of Mental Health. The Institute of Mental Health established the Psychopharmacology Service Center and assigned to it the job of promoting, by every legitimate means, increased research in these areas, including standardization of drugs; evaluation of their therapeutic efficiency; development of new drugs which will do a better and safer job, if possible, than present drugs; and establishment of a central clearing house of information to be available to all researchers on what has been done in this field. In addition, the Center is collaborating with the Veterans Administration on its large-scale tranquilizing drug research program. This year, the Congress has appropriated \$2 million for continuation of the program.

Thus we see that chemotherapy has progressed from its first hesitant steps to emergence as a major part of the total Federal medical research effort. Not even the most brash prognosticator would dare to make a flat prediction as to our future in this field. Of three things I am quite positive:

First, we ^{may} ~~will~~ never see the day when a newspaper headline will declare that cancer or mental illness has been "conquered" -- or any of the other major chronic diseases, for that matter.

Second, we will see, year by year, a gradual chipping away at the walls of ignorance that lie between man and his understanding of these disease processes. Through programs such as those we have just discussed, we will see bits and pieces of new knowledge coming out, being correlated and compared, and being used to pursue treatment and cure of certain types of chronic diseases. Ultimately, I am sure, the pressure of all these "small breakthroughs" will bring us to the eradication of many of today's greatest disease killers.

Finally, with the continued and strengthened support of research, based on enlightened public response, that "ultimate day" to which I just referred will move closer and closer. In my talks with the people who have charge of these chemotherapy programs for the Federal government, and in my observation of how they have been put into effect, it is clear that there is splendid cooperation and an integrated total effort directed toward the prosecution not only of these "target" programs but all research in the life sciences. You whose field is chemistry have great contributions to make to the future, as you have to the past.

To each of you as individual members of the American Chemical Society, your Rhode Island Section, and as part of the 82,000 national membership, I congratulate you and wish you the greatest success in the future. Thank you.