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Mr. Chairman, ladies and gentlemen. It is an honor, indeed, to be asked to give the Linsley R. Williams Memorial Lecture, and to participate thereby in the Laity Series of the New York Academy of Medicine. The fruitful career of Dr. Williams included contributions of great importance to the modern structure of the New York Academy of Medicine, which he served as full-time director, and also to the leadership of the National Tuberculosis Association.

His deep interest in the promotion of medical education, in preventive medicine, public health and social welfare, and in the development of basic research to the accomplishment of the goals in these several fields, would have led him quite naturally to the problem of incurable cancer. In the 20 years since his death, tuberculosis – which had challenged his talents – has begun to fall from its great importance as a public health problem. First, because of the great advances in hygiene, and, more recently, because of the happy discovery of chemical agents which specifically interfere with the growth of tubercle basalis in the human body.

And today, the condemnation of public health control directly toward prevention were possible, and early detection of cancer, and the application of chemotherapy to the problem of disseminated cancer, promises to alter the centuries-old pessimism concerning the problem of cancer in man.

Your invitation to give this lecture as a part of the Laity Lecture Series represents an additional challenge. Any discussion on the chemotherapy of cancer must be based upon results so recent as to make clear that a lecture on this subject, but a decade ago, if attempted, would have had to be written in imitation of Jules Verne, rather than in the form of a scientific treatise. Your Dr. Iago Galdston, in a masterful short history of chemotherapy, entitled, “Behind the Sulfa Drugs,” published some 11 years ago, pointed out that the term “chemotherapy,” which is usually interpreted as the treatment of disease by means of chemical agents, had been incorporated for many years in the implications of the word yatrochemistry – the science of chemistry applied to medicine.

Paul Ehrlich, however, had something different in mind. He coined the term “chemotherapy” – not to imply that chemistry was to be utilized in the treatment of the disease, but rather in the destruction of the specific disease-producing living agents within the body of the diseased being.

As Dr. Galdston has phrased it, the aim of early chemotherapy was inner-sterilization – actual sterilization within the cell itself.

Our discussion tonight, therefore, is based upon research – most of it no older than 10 years, and as recent as this moment. But it is only the breakthrough which has come in these last few years. What has been accomplished is based clearly upon contributions, made through the centuries and from a variety of disciplines, by individuals and institutions scattered over the world. The essence of the most important direction of current research in cancer chemotherapy is a phenomenon of biological antagonism.

In his classic paper on the biology of fermentation in 1857, Pasteur laid the foundation for this concept. Pasteur postulated also that a living cell can be inhibited specifically by a definite substance in a selective manner. It was Ringer, in 1882, who described in chemical terms the interference between specific ions in biological systems. In 1907, Ehrlich published his theories on specific therapeutics and founded thereby the present-day field of specific chemical inhibition – or to use more modern terminology, anti-metabolite phenomena.

We may define, now, for our purposes in this discussion, the term “metabolite” as a biologically active chemical substance necessary for the growth of the cell. More recent is the development of the concept of competitive antagonism. In 1935, Dickens gave the first clear-cut illustration of the adsorption of a metabolite analog, which he explained on the basis of structural similarity of the dyes he employed, and co-enzyme. A negative complex resulted from the replacement of co-enzyme by dye.

In the following year, Clark explained competitive drug antagonism on the basis of the structural similarity between pairs of mutually antagonistic drugs. The illustration of the metabolite, anti-metabolite nature of sulfonamide inhibition accelerated greatly the progress in this direction of research. The theoretical and experimental contributions of D.A. Wooley hastened application to the cancer problem, and helped to overcome a delay explained by the pessimism which had hindered research in cancer for centuries.

It will be appropriate to introduce these remarks considering the chemotherapy of cancer by a few comments on the treatment of cancer by methods of proved value. The word “cancer” today, it is agreed by authorities in this field, is a term used to cover a great many diseases, arising perhaps from a multiplicity of unrelated causative factors of widely-varying biological characteristics and environmental influences. Wide variation exists, too, in the life history and biological behavior of these many different forms of cancer – and we should expect, important differences in response to treatment.

We may compare the different forms of cancer to the many different forms of infectious disease, and we find them unrelated – as is typhoid fever, for example, to meningococcal meningitis. ... These are different diseases giving different problems and necessitating different forms of treatment. Although here in the field of infectious disease there exists today the hope which eventually may be found in the field of cancer chemotherapy that a broad spectrum single substance may affect many different forms of cancer which apparently have different ideological backgrounds.

No discussion of a new approach to treatment should neglect the fact that thousands of patients have been cured through the techniques of the surgeon, and to a lesser extent those of the radiologist. The surgeon removes from the body those masses and attached organs which can be removed with safety after the diagnosis of malignant tumor has been made. The radiologist uses an instrument which results in the destruction of those forms of cancer which are sensitive to irradiation.

Whenever it is possible [the goal is] to destroy the tumor without calling upon the normal tissues to pay a price the body cannot afford. As we now know, hormones and chemical agents presently available are, when they are effective, destructive agents too – but in a more satisfactory manner. The ideal treatment for cancer would be one which would supply the malignant cell with the lacking enzyme, the absent trace element, or the needed biological material which would permit the abnormal undifferentiated tumor cell first to mature, and then to be transformed into normal tissue by those mechanisms which maintain under normal conditions the contour and function of the components of the body.

We recall here the extraordinary remodeling of bone ... in the classic experiments of the late Dr. S. B. Wolbach. And we conceive in the case of cancer chemotherapy of a similar remodeling and eventual transformation of a chemically treated tumor mass, now composed of mature cells and tissues as a consequence of the action of the chemical agent. Such an attack would be aimed at the very essence of the cancer problem if there be one such, or to the common denominator of all the different causes of the malignant process. Such an approach, unfortunately, has not yet been made on a sound experimental basis.

Ehrlich's definition of chemotherapy, inner-sterilization, will be enlarged in this presentation to include the dissolution of the cancerous process by chemical agents administered to the patient, as well as the possibility of the transformation of the malignant's tumor to normal tissue – now so molded and fashioned, as to fall in with the structural and functional needs of the body. A transformation produced by the administration of chemical materials having the exact biological attributes required for the purpose. That, then, is the eventual goal of the most rational form of chemotherapy of cancer, and one which certainly has not been achieved.

In our preoccupation, therefore, in the search for new forms of treatment of cancer, we must not neglect the great strides which have been made in the application of surgical and radiological techniques on the basis of early diagnosis and prompt treatment of the malignant tumor. And in the end, acceptance of the assumption that cancer is a covering term for a multiplicity of unrelated diseases. There is the implication that we must search not for "A" cure for cancer, but rather for a series of cures for the various kinds of disease grouped under the term "cancer."

The need for new methods of treatment is made apparent in several ways. We recognize our inability today to diagnose the presence of cancer in every instance early enough to permit surgical removal before the time that spread or metastasis to distant parts of the body has taken place. There is still no accurate cancer diagnostic test which will permit the demonstration of the presence of cancer somewhere in the body by the examination of a specimen of blood or of other tissue or fluid from the body.

This is not to be confused with the extremely valuable Papanicolaou smear tests, which are of such tremendous practical importance today in the diagnosis of certain forms of cancer which can be reached through the external body orifices or which demonstrate themselves in other matters.

Then, too, there are a number of kinds of cancer which from the very beginning appear to be widespread throughout the body and therefore untreatable by the techniques of surgery and radiation. This group includes acute and chronic leukemia, the various forms of lymphoma or lymphosarcoma, and Hodgkin's disease. The disease acute leukemia, for example, is characterized by the virtual replacement of the bone marrow and invasion of many of the important organs of the body by cancer cells arising originally from those which form the white blood cells of the body.

This occurs much more frequently in the child than in the adult; it is responsible for death if not treated within a few weeks to a few months after the onset of the disease. Only a small number of patients untreated live as long as a year. This disease is still an incurable disease despite the great progress in chemotherapy of acute leukemia.

In the chronic forms of leukemia – lymphoma and Hodgkin's disease – the course may run from months to many years, with varying degrees of discomfort depending on the rapidity of the spread of the tumor and the extent and location within the organs of the body occupied by the cancer. For these forms of cancer, incurable or untreatable by surgical techniques, new treatments therefore have had to be developed. All the more, since an estimated 50 to 65 percent of all patients with cancer today cannot be cured by methods of proved value in the greater percentage of patients.

It has long been the hope of those concerned with the sick that chemicals would be found which, when taken by mouth, or put into the body, would cure the disease widespread throughout the patient. Galdston credits Paracelsus, who lived from 1493 to 1541, for having initiated the science of chemotherapy – a science which was really founded as a science 400 years later by Paul Ehrlich, Paracelsus spoke with the intuition of genius of the chemical Arcana to drive out the venoms of specific disease.

The contributions of Ehrlich have the greatest influence on the chemotherapy of infectious disease, but so fixed has been the pessimism throughout the ages concerning the cancer problem, that even as late as 1945, many of the leaders of cancer research paid scant attention to the oft-dreamed-of possibility that cancer chemotherapy could become a reality. Some of this was based upon the disappointment arising from the failure of even the greatest chemical minds to devise, research, and to demonstrate important chemical differences between the cancer cell and the normal cell.

I am reminded of the remarks of Shields Warren at the second conference on folic acid antagonists in the treatment of leukemia held in Boston in 1951. He recalled the meeting for the Association of Cancer Research some 20 years before. There was a long series of papers on how to produce cancer in mice, and large lecture hall was crowded. This was the era of

carcinogenesis, and great progress indeed had been made in the provision of pure chemical materials which, when treated properly, could cause cancer in the mouse.

This part of the scientific program was followed by a paper on an attempt to cure incurable cancer in man. Before the speaker could reach the podium, the hall was virtually empty. Dr. Warren pointed out that this was merely an indication of the lack of any lead in the field of cancer research in 1931, which looked as though there might be a breakthrough into the problem of disseminated cancer.

How different is the outlook today, and on what does this change depend? The first important contribution came, interestingly enough, not from the use of the pure chemical compounds, but through the discovery that hormones, which act as chemical substances, provide one great direction of research in chemotherapy. That hormones, concerned particularly with the male and female sex hormones, and this great direction today is concerned with the alteration of the structure of the male and female sex hormones in order to deviate the toxic or untoward effects of these materials, and to accentuate at the same time, the cancer-destroying powers of these materials.

A landmark in the chemotherapy of cancer was the research of [Charles] Huggins in 1941 in the control of cancer of the prostate gland by the removal through castration of the male sex hormone stimulus to the growth of prostatic tissue. This observation suggested the use of castration, and then male sex hormone therapy in the treatment of women with cancer of the breast. The use of ACTH, and later cortisone, in the treatment particularly of leukemia and lymphoma, represents other applications of hormone therapy in the chemotherapy of cancer.

The first chemical compound actually used to produce changes in widespread cancer came through a byproduct of research designed for an entirely different purpose. Nitrogen mustard, one of the important halogen gases and materials of the war [World War II] was found in experimental animals to have a profound effect upon the spleen and the lymph node tissue. Those concerned with this research, and with a study of anti-cancer materials in general, seized upon this observation and found that this poison material, when used appropriately, in dosage which the human body could tolerate, was capable of bringing about temporary, striking improvement in certain forms of lymphoma and Hodgkin's disease and more rarely in other forms of cancer too.

The first important chemical compound which seemed to have a close relationship to an actual important chemical material needed for the growth of the cells of the body was the folic acid antagonists. ... A whole series of these folic acid antagonists are now known to have important effects in preventing the conversion of folic acid to carcinolytic chemical compounds. And these, when used in man, are capable of causing important temporary improvement in patients with acute leukemia and several other forms of widespread or so-called incurable cancer.

The importance of the discovery of folic acid antagonists as carcinolytic chemical compounds lies in the fact that the whole field of metabolite/anti-metabolite research was given tremendous impetus by the demonstration that an anti-metabolite related closely in structure to a substance necessary for the growth of cells was indeed an effective anti-cancer agent. This work,

chemically produced through the laboratories of the American Cynamide Company under the direction of the late Dr. Yellapragada SubbaRow has opened new vistas, then, in cancer chemotherapy.

Not long afterward, the demonstration from the research in basic science of men such as Dougherty and White, found the effects ... on the spleen and lymphocytes, led to ... treatment first of children with acute leukemia, and later other forms of cancer. We now know cortisone is an effective hormone for temporary improvement in acute leukemia – particularly in children, but also in adults.

How do we select chemical compounds today? There are several possibilities; we may begin with a rational approach, and this we shall consider briefly a little later. Or we may take the suggestion made by many people that every chemical compound on the shelf of every chemical factory or laboratory be subjected to chemical analysis and biological screening. If we are to take this second course, it is obvious that we must have a screening method which would tell us accurately that a given chemical has anti-cancer powers. It must be accurate enough so that further work, which is long, tedious, expensive, and time-consuming in manpower hours, will not be wasted. We also want to have a screen which will be so effective that important chemical compounds will not be missed. This problem is obviously not a simple one, and it has not been solved.

There are several screening methods which are in use today. Under the chairmanship of Dr. Alfred Gellhorn of Columbia University, the special research commission of the American Cancer Society studied the action of 27 compounds in 69 screening systems. A whole series of investigators in various parts of the country participated in this study. Many different biological systems gave interesting responses, but in general it was found that the action of the chemical compound on the transplanted tumor in the mouse in pure-bred strains gave the most valuable information, although correlation with anti-cancer activity in man is still far from constant or satisfactory.

These pure-bred strains of mice which are employed come to us through the long years of research ... in the Bar Harbor Research Laboratory. From these Jackson Laboratories have come not only the pure-bred strains of mice which make this work possible, but also the many different forms of spontaneous tumors in the mice which were then transplanted for generations until constant or relatively constant conditions could be obtained for screening purposes.

The pioneer screening program of Dr. Murray Shear at the National Cancer Institute gave the methodology which helped accelerate similar programs elsewhere. The largest program of this kind in a private institution has been carried on for 10 years under Chester Stock and Dr. Rhodes in the Sloan-Kettering laboratory. Smaller, more specific programs directed toward the careful study of certain classes of chemical compounds have been carried out in laboratories of industry, and in organizations such as the Children's Cancer Research Foundation in Boston.

The first method of the routine study of the action of chemicals chosen without discrimination on the growth of selected mouse cancers growing in the mouse has now been brought to the point of study and analysis, and sufficient thousands of compounds have been so studied. On the basis of

a very small yield, it is now possible to create new chemical compounds, analogs of those which have proved to be of interest in the mouse study systems.

There is another method which has been of great interest to workers in the field of cancer chemotherapy in the last few years. This concerns the growth of cancer removed from the human being at operation and grown in the Syrian hamster or in the Chinese hamster or in the white laboratory rat. Hundreds of such tumors have been transplanted to the new host – the hamster. A small number of these human tumors can be grown quite readily, particularly if the hamster or the rat is treated by irradiation or injected with cortisone at the time the human tumor is transplanted.

Attempts are now being made to standardize this test method to permit the study of the action of chemical compounds on human tumors grown in this abnormal environment. It must be emphasized that this new environment does differ in many important ways from the original environment of the tumor. No success can be reported at this time, because of grave technical difficulties. If these can be overcome, and there is reason to believe such difficulties will be overcome by research presently in progress at a number of institutions, it may be possible to achieve the hope so often expressed that the ideal chemical compound may be selected for a given patient after the study of all available anti-cancer substances against tumors grown in the hamster or the rat from the patient whom we now want to treat more specifically than we have ever been able to before.

If this is realized, there will be much more rationale in the choice of the chemical compound in the treatment of a given patient. We will be treating the exact host as well as the type of tumor from which the host suffers.

Before any anti-cancer substance may be used in man, its toxicity and its impact on the brain, the kidneys, the liver, the vascular system, and other parts of the body, the metabolic activity of the chemical compound – its absorption, excretion, and metabolism in the body – must be determined by careful laboratory work. It is hoped that many more well-equipped and splendidly staffed screening centers and pharmacology study centers will be established in this country in order to produce the basic data so badly needed before anti-cancer agents can be chosen for use in man with better accuracy than is possible today.

There are other methods which are employed in the choice of anti-cancer chemicals. Microbiological test systems which make use of the growth of bacteria in artificial media – the exact constituency of which is known – contribute greatly to our knowledge of the mechanism of action of those chemical compounds proved to be of importance against cancer by any one of the several approaches utilized. This combination of biochemistry and bacteriology has yielded important data of value to cancer chemotherapy. The value is advanced by the rapidity with which data of this kind can be accumulated.

What kinds of chemical compounds are now of interest in the field of chemotherapy? There are two broad classes which have proved to be of interest on the basis of effectiveness either against tumors in the mouse screening systems or against tumors in man. The first great class of

compounds we shall term the anti-metabolites; the second are the cytotoxic agents such as nitrogen mustard.

The action of chemical agents in general against cancer may be ascribed to an interference with a living process of the cell. Such interference may take place at any stage or at all stages in the development and function of the cell. If the cells are arrested in mitotic activity, we may not conclude that the chemical necessarily acts by interference with mitosis.

The nitrogen mustards, for example, appear to possess the character of cross-linking protein whereby cellular-functioning proteins are immobilized. This may be called their structural or physical effect. By binding self-hydro enzymes that also interfere with cell growth, vital respiratory and oxidated enzymes are blocked, causing what may be called inhibition of chemical biocatalytic processes.

Unfortunately, every chemical compound so far proved to be of value in the treatment of cancer in man has encountered sooner or later the phenomenon of resistance on the part of the cancer cells, which had at first been sensitive to the anti-cancer chemical. Research indicates that this phenomenon, which is similar to that observed in the chemotherapy of bacterial infections, may be explained on the basis of mutation of the cancer cells which survived.

It is quite possible that even the most effective chemical agents may kill only 99 percent of the cancer cells when patients improve markedly and return to a state for a short period of time indistinguishable from normal. This is seen most strikingly in those patients with acute leukemia, who show these temporary striking improvements. It is quite possible that the 1 percent of cells which remain, or which cannot be recognized by any of our diagnostic methods, have acquired resistance to the chemical agent to which all of the other cells had succumbed. And from these resistant cells, there will be formed further growth – and widespread growth – of the malignant tumor.

Theoretical possibilities which exist in explanation of this phenomenon of resistance concern themselves with: 1) a possible alteration in the permeability of the cell to the anti-cancer agent; or 2) to possible alterations in the utilization of the chemical which may become food for the cell instead of a poison. And finally, an explanation is offered concerning the utilization of alternate metabolic pathways by the cell which may thus synthesize successfully nuclear protein by means of a pathway not blocked by the anti-cancer agent.

This solution of the problem of resistance represents one of the most important in cancer chemotherapy if temporary gains, remissions, or controls of certain forms of cancer are to be transformed into permanent cures. The site of action of anti-cancer drugs may be studied now on the basis of past successful experience of the past 8 to 10 years.

A retrospective glance at the experimental data gained after the demonstration of anti-cancer effects by several different classes of chemical compounds suggests the chemicals may act in any one of several different ways. There may be an interference with a conversion of folic acid ... required for the synthesis of nucleic acid precursors. ... This does not imply that folic acid causes

leukemia, or cancer; folic acid is merely one of the important cofactors required for the growth of cells.

There may be an interference with the synthesis of nucleic acid from preformed purines by substances such as 6-mercaptourine – purinethol. Or there may be an actual destruction of already-formed nucleic acids, as is the case with the nitrogen mustards and related compounds.

Despite the great advances in our knowledge of the chemistry of the cancer cell, and the lessons learned from the action of empirically discovered chemical compounds with anti-cancer activity, it is still impossible to synthesize on the basis of theoretical considerations alone the ideal cancer compound, and know that it will, with certainty, be effective when tried. Nor is there sufficient understanding to permit the assumption that a chemical compound which will be effective against one kind of tumor will work also against others.

Recent discoveries that certain viruses act as anti-cancer agents may lead to studies which will show that they act not as living biological entities, but merely on the basis of their chemical structures. The latest promising studies of new chemotherapeutic agents have come from the action of antibiotics against certain forms of cancer in the experimental animal. Antibiotics ... have demonstrated, at least in the mouse tumor systems, of striking anti-cancer effects. This discovery necessitates large-scale screening of every known antibiotic and a search for new tools in an attempt to find the anti-cancer action of new antibiotics to determine the exact chemical components of the antibiotic responsible for this anti-cancer action.

Such a program can be based not upon a rationale approach, since the element of fortune plays the dominant role in the discovery of an antibiotic. Such a program, however, must be based upon expert knowledge, skill, and the availability of equipment. I think we may anticipate, without question, great progress in the search for anti-cancer antibiotics in the next few years.

The chemotherapy of human cancer is now an achievement. Chemotherapy has advanced to the stage of the development of several chemical compounds actually now used in the practice of medicine. These include folic acid antagonists, such as Amadoptrin and Methodextrate, Nitrogen Mustard, Purine Antagonists and Analogs such as 6-Mercaptourine, Purine Ethol, a series of mustard-like materials, and a whole series of related compounds. All anti-cancer effects reduced by chemical components are temporary in man, with effects lasting from weeks to months – and only occasionally for periods as long as six years.

The vast majority of these beneficial effects have been found in the acute and chronic leukemias; in Hodgkin's disease; and in the lymphoma group of cancers. A small number of beneficial effects have been produced in tumors such as the neuroblastoma, cancer of the breast, and of the prostate, certain tumors of the brain, and scattered apparently unrelated cancer in various parts of the body. Such clinical investigations are still in their infancy; there will be great progress in the next few years in the search for action against cancer in man of these anti-cancer agents now available.

A few examples of the effect of chemical agents may be given. Acute leukemia may be profoundly affected by folic acid antagonists, ADPH cortisone, and purine analog – either singly, in combination, or in sequence with marked improvement resulting in from 50 to 70 percent of children so treated. Such an affect may be characterized in a return to a condition frequently indistinguishable from normal for a period of weeks, months, and, in rare cases, for years.

Here, too, beneficial effects are terminated by the acquisition of resistance on the part of the leukemia cell. Patients with widespread metastases' in cancer of the breast, or of the prostate, may be improved markedly for as long as three or more years following the use of appropriate hormones. A number of different chemical agents have added comfort, if not periods of survival, to those suffering from various forms of lymphoma and chronic leukemia.

There is still no chemical cure for those forms of cancer which cannot be cured by surgical or radiological techniques. Clinical experience of the last few years, however, has shown that chemical agents may, on occasion, cause previously inoperable cancers to become operable, and previously radio insensitive cancers to become sensitive. It is in this direction that great progress may be anticipated by combined surgical, radiological, and chemical treatment of disseminated cancer. The use of chemical agents as part of total care of the patient with cancer has improved greatly the lot of even of those patients with tumors which do not respond to chemical agents because of the greater amount of care given to the patient as part of such a program.

In conclusion, may we speak of the dream of scientists and doctors over the centuries of the treatment of cancer by chemical agents? May we say that this dream has been realized with the accomplishment of some good results, although they are still of only temporary value? Chemical substances are available which when administered to patients with disseminated cancers of certain kinds do produce temporary shrinkage and even disappearance of widely disseminated tumor tissue.

A continued search, making use of either the empirical or the rationale approach is certainly justified by this achievement. A solution to the problem of resistance must be found if more-lasting results are to be obtained with the agents presently available. The methodology of chemotherapy, borrowed from many other disciplines, has been whipped into shape within the last few years to facilitate the scientific search for anti-cancer materials.

The possibility exists that an unpredictable discovery may take place at ANY time. Those concerned with progress in this field, however, must depend upon arduous routine; interminable screening, and constant testing of hypotheses to be discarded as fast as they are found wanting. There is no shortcut to this work. The availability of scientific methodology used by competent workers in this field points out the requirements for the testing of any claim for anti-cancer properties of biological materials or chemicals.

No date can be set for the eventual discovery of the many cures for the many different forms of cancer. The great progress of the last 10 years justifies the optimistic conclusion that such cures WILL be found for many forms of cancer through the use of chemical agents or hormones. A plea is made for peace and quiet as well as support for research workers in this field.

The national advisory cancer council of the United States Public Health Service, through the director of the National Cancer Institute, has established a committee on chemotherapy of cancer, now sponsored equally by the American Cancer Society and the Damon Runyon Association, and supported, too, by numerous organizations and individuals working in this field. Its purpose is the acceleration of progress in the chemotherapy of cancer and the development of new techniques for the rapid communication of results of research to all individuals and institutions in the world engaged in this program of voluntary cooperation.

There will then be no one V-Day when the cure of cancer will be achieved. Progress will be achieved in spurts, with great unevenness and irregularity. Achievements in one field and then another, indeed, may become so numerous that they will, it may be hoped, pass almost unnoticed, except by the scientific world and the patients who are helped. Anti-cancer compounds are being used in daily practice now, producing effects which would have aroused intense excitement a scant five or seven years ago.

The availability of master craftsmen, as Huggins has called them, of expert and trained scientists in increasing numbers, of adequately equipped laboratories and hospital wards, and of the resources necessary to support a research effort of a magnitude never before attempted in the history of medicine give promise of eventual success in the search for the many cures for the many different kinds of cancer afflicting man.

This controlled optimism is based upon the conviction that the accomplishments of the last seven to 10 years, based upon the scientific advances of the centuries, have provided the directions for research in the treatment of disseminating or incurable cancer. We must remind ourselves that only by carefully controlled research, by critical scientific methodology, and by the integration of the activities of free research workers from the many different disciplines of medicine, chemistry, physics, and biology can further progress be made.

But the breakthrough has occurred in the chemotherapy of cancer in these past few years. Those who labor in the laboratories of organic chemistry, of experimental pharmacology, or physiology, far removed from the patient, as well as those physicians who are concerned with this new venture in treatment, are supported by the knowledge that widespread of cancer in the human body can be destroyed, even though not completely, and be markedly effected, even though temporarily, by the use of chemicals administered to the patient.

And for the patient, suffering from what he knows is cancer beyond the reach of present methods of treatment of proved value, there is the assurance that this activity in the world of research and chemotherapy of cancer guarantees to him that he will not be embattled.