In 1775, I have read, an organized group of Americans under General Richard Montgomery briefly visited Canada, but because of poor interpersonal relationships between the tourists and the natives there was a certain air of hostility about the entire meeting. Now in 1963 a considerably larger contingent of U.S. citizens has come to Canada, and the friendliness of the reception accorded them and the ease of communication among all of us are happily acknowledged.

Since the founding of the American Association for Cancer Research in May, 1907, there have been profound changes in the emphasis on scientific research. The acquisition of knowledge and its application to human needs has grown beyond the expectation of even the most optimistic, and it is apparent that on the future healthy progress of science depends not only the development of society, but even its maintenance. The problem at the moment seems to be that there are quite conflicting ideas about the way to achieve scientific progress. Scientist leaders, scientific administrators, Congressmen, private foundations, our friends and patients all have suggestions and plans. In the frenetic heavings and haulings the research worker may feel that he is confronting Canadian Stephen Leacock’s hero who “flung himself from the room, flung himself upon his horse and rode madly off in all directions.”

We present an inviting target to the planners because it is only human to hope that judicious prodding may hasten the control of cancer. I would be all for this type of stimulus were it not for the implication that the prodder really knows where I should go, and I doubt this. We have learned many facts about cancer, and I believe that equally significantly we have acquired some guiding principles for this field of research. I would like to trace with you the growth of knowledge about cancer and the emergence of a philosophy of cancer research from the early part of the 20th century to the second World War, from the atomic revolution to the biological revolution, and now.

When our Association was founded (68), the charter members included outstanding experimental biologists such as Leo Loeb and George A. Clowes, keen students of human neoplastic disease such as James Ewing and Frank B. Mallory, and skilled clinicians such as George W. Crile and William B. Coley. The breadth of interests represented by these men gives a clear indication of their recognition that the concern of cancer research necessarily includes the gamut of biological science. They were living and working at an extraordinarily provocative moment in scientific history. Roentgen’s discovery was well beyond the photographic plate-fogging stage and was into the phase of diagnostic application and of tissue destruction for unwary radiologists; Ehrlich was spinning alluring hypotheses and making progress in pragmatic chemotherapy (to say nothing of selecting several mouse mammary tumors which have transplanted his name to every cancer research laboratory throughout the world); Fischer had made observations with an azo dye which laid the foundations for laboratory study of chemical carcinogenesis; and Yamagiwa and Ichikawa, Kennaway, Cook, and Hewett, and many others were working on tar and carcinogenic hydrocarbons which now put fear and trembling into cigarette manufacturers (but not, alas, into cig
the advent of atomic energy, which was introduced some years culminated with an unprepared world on August 6, 1945, at Hiroshima. Since then cancer research has grown tremendously. The only thing which can digest the vast recordings of work done is the Honeywell 800, a mammoth computer housed in air-conditioned splendor at the lovely new National Library of Medicine. If you can formulate your question precisely, MEDLARS (50) (an acronym for Medical Literature Analysis and Retrieval System) will quickly search its memory, which it has been stocking at the rate of 140,000-160,000 scientific articles per year, and deliver an impeccably typed list for you. If your question is diffuse and inept, MEDLARS will produce a wallpaper-sized document, with a sneer.

Although much of what we have done in the past 15 years cannot yet be prospectively evaluated, certain aspects have been clearly relevant. The work on chemical and physical carcinogens has been made increasingly pertinent, not only to those in particular industries but to the population at large (26, 56, 60). Issues on tobacco tar, air pollutants, radiation, and food additives have been examined, and epidemiologic research has been shown to be a powerful heuristic technic as well as indicating public health measures. Chemotherapy in cancer has had a revival since 1940 and has overshadowed most other areas of cancer research in terms of the lavishness of financial support and the effort expended (84). The field has been bright with the accomplishments of individuals as, for example, the 4-H club of Huggins, Haddow, Hitchings, and Heidelberger, who, with many others whose names do and do not begin with H, not only contributed pragmatically to the management of human neoplastic disease but also provided tools for fundamental study of normal and neoplastic growth.

During these past 15 years, the work of Furth (19) and Foulds (17) has increased our appreciation of the progression of tumors from dependency through conditional phases to autonomy, and Papanicolaou’s exfoliative cytology approach has indicated that the progression of carcinoma-in-situ to invasive cancer is representative of this phenomenon in man.

And radioactive isotopes, electron microscopes, ultracentrifugals, spectrometers—mass, ultraviolet, infrared, scintillation, fluorescent—all these and more have been applied with intensity to the investigation of the biochemistry of the cancer cell (1, 7). Although no unequivocal demonstration of a qualitative difference from the normal cell has been made (24), the myriad static and dynamic biochemical characterizations contributed to the groundwork for the Third Scientific Revolution, now upon us. This, the new approach to biology,
has already taken impressive strides toward the integration of basic knowledge in physical, inorganic, and macromolecular chemistry with genetics, virology, physiology, and biochemistry, leading to a reinterpretation of biological phenomena at the molecular level (22). The vitality of the concept is felt in the hum and glow of work in all areas of biological study; soon the social sciences will feel the warmth as applications of the findings to the maintenance and restoration of health are made; and citizens and statesmen must take heed, for one can even glimpse the potentialities for distortion of the new biology to evil purposes.

At this moment in history, when progress is being made toward a unification of chemistry, physics and biology, is cancer research participating and contributing in this trend? It is. Consider, for example, this year of glory in the marriage of genetics and biochemistry (18). The concept (72) of the flow of information from the DNA molecule through the mediation of messenger RNA, then the interaction of transfer RNA and messenger RNA to the synthesis of specific protein molecules has been extensively subjected to experimental validation. Evidence has been obtained for a triplet code of the purine and pyrimidine bases which directs the incorporation of the twenty amino acids into polypeptides (48, 51, 62). There remain a number of questions regarding universality and ambiguity in the code, but in Crick's words, "... it is not unreasonable to hope that all these points will be clarified in the near future, and that the genetic code will be completely established on a sound experimental basis within the next few years" (10).

Much of the earlier work defining the genetic mechanisms for protein synthesis was done in microbial systems, but the past year has seen the broad extension of the conclusions to mammalian cell systems (3, 45, 46, 52, 73, 74). Thus it has been found that natural and synthetic messenger RNA's stimulate amino acid incorporation into polypeptides in subcellular extracts from rat liver, human and rabbit reticulocytes, normal and leukemic leukocytes, and human and mouse plasmacytomas. Of particular pertinence to the fundamental issue of "what is cancer" has been the demonstration that the protein-producing system of tumor cells responds to artificial messenger polynucleotides in the same manner as normal cells. The available evidence at this moment suggests that the secret of cancer is not to be found in a misreading of the code by the transfer RNA's.

If it is now possible to direct and stimulate the incorporation of amino acids into protein in subcellular systems, and if the ribosomes, transfer RNA's and attendant enzymatic equipment of tumor cells respond as do normal cells to synthetic and natural messenger RNA's, is there not the possibility to direct "wisely" the synthesis of protein in intact neoplastic cells? What vistas does this open for rational therapy? But can a macromolecule cross the cell membrane, or, if it can, could it modify normal cell function before being destroyed by specific nucleases? The transformation and transduction experiments in bacteria give an affirmative indication, and more recently it has been shown that naked viral nucleic acid can produce tumor transformation in intact mammalian cells (11, 30, 38). Further, synthesis of bacterial protein has been achieved in chick cells by the addition of an extract from E. coli to chick fibroblasts in vitro (9), and human cells in tissue culture have synthesized a new enzyme under the direction of an exogenous DNA (66). Although these are still pioneering steps and are far, far from the goal of therapeutic application, it is clear that a new pathway has been found and the first blazes have been struck.

We have mentioned the use of new instrumentation in cancer research; now I would like to describe an old instrument that has been recently applied to a particular area of cancer study. In clinical medicine we use it often. It is known as the retrospectoscope. With it, the physician, who sees a patient previously observed and treated by many other doctors during the natural history of his disease, is always wiser than his colleagues, for he can easily see their errors. The retrospectoscopes have been trained on viral carcinogenesis and have been working so well that Drs. Rous, Shope, Furth, Beard, Stanley, Gross, the late Dr. Bittner were he here, and others may sometimes find it hard to believe the difficulties they have had in the past in convincing the scientific community of the relevance of their observations to the problems of cancer. Be that as it may, I will take the liberty to cite concepts regarding the tumor viruses as another indication of the inextricability of cancer and general biological research (25, 27, 40, 49, 59) (and I'll say it as though I knew it all along).

In 1898, Sanarelli suggested that the rapidly lethal myxomatous neoplastic disease in domestic rabbits was due to a virus. There was, however, reluctance on the part of students of cancer to accept that the tumors, which morphologically looked like tumors, could be transplanted, and did metastasize, were, in fact, tumors. The conceptual problem presented by the basic assumption that the cause of cancer is not known and therefore a cancer produced by a known cause such as a virus...
cannot truly be cancer, gradually diminished. In its stead another hypothesis gained support, namely, that tumor viruses are a class unto themselves and quite distinct from agents which produce infectious diseases. This is now under critical re-examination as similarities between the infectious disease and oncogenic viruses accumulate. Among these may be mentioned the following: (a) It had long been thought that tumor viruses, unlike others, were species- and even strain-specific. This has been amply disproved by the demonstration that the Rous chicken sarcoma virus can produce tumors in rabbits, the Gross murine leukemia agent can produce the disease in rats, and the polyoma virus has a broad spectrum of rodents susceptible to its cytocidal and oncogenic effects. (b) The chemical constitution and morphology of infectious disease, tumor, and bacterial viruses have many common characteristics. The adenoviruses and the polyoma virus, for example, are DNA viruses and their localization in the nucleus as well as their intracellular crystallization patterns is similar. (c) It has been known for some time that there are “defective” viral agents which require the replication of a “helper” virus to make possible their own reproduction. Recently, it has been reported that there is a strain of Rous sarcoma virus which cannot generate the production of new infectious virus in the absence of the intracellular multiplication of a “helper” virus. (d) Tumor viruses can produce diseases other than cancer. Thus, Rous showed many years ago that the sarcoma-producing virus which bears his name causes a hemorrhagic disease without any neoplastic characteristics in certain strains of adult fowl, and Duran-Reynals showed the susceptibility of young chicks to the generalized hemorrhagic disease due to the same agent. More contemporaneously, it has been shown that the polyoma virus more often causes cell death than neoplastic transformation. The recognition of the potentiality of the oncogenic viruses to cause cellular disturbances other than neoplasia carries the implicit possibility that viruses which usually cause infectious disease syndromes, or even are latent, may produce tumors. This now has been demonstrated by Trentin, Huebner, and Eddy who, with their associates, have independently recorded the production of malignant tumors in hamsters with strains of human adenovirus and a simian virus (14, 37, 67). These convincing experiments are disconcerting in the suggestion that tumor viruses are not unique in their capacity to induce tumors but that the neoplastic transformation may be one of the types of cellular response that can be elicited by a wide variety of infective nucleic acids.

It is clear that tumor virology is very intimately a part of the whole field of virology. Study of the chemistry, biochemistry, anatomy, mechanism of action, transmission, ecology, pathology, prevention and therapy of any virus may, and does, have great significance for unrelated diseases including cancer.

But what of the clinical investigator? Surely he must be a very categorical fellow. His field of study can only have relevance to cancer in man. Is this so? Is clinical oncology entirely separable from the broad study of human health and disease? Is there no real partnership between clinical and laboratory research? The answer to rhetorical questions is always obvious, but let’s consider some evidence.

The clinical investigator has advantages and disadvantages. He is limited because his subject is an ill human being and we all know that suffering pervades the whole body. The clinical investigator’s conclusions then must necessarily be qualified because of the complex cell, organ, and system interactions in a patient, to say nothing of variables introduced by the uncontrolled genetic and environmental background. Further, it is well to remember that humaneness frequently is a deterrent in clinical studies, as it should be, for when a patient becomes a purely statistical experience he is no longer receiving proper medical care. These factors make clinical investigation desperately difficult so that good studies merit appreciation. But the clinical investigator has certain distinct advantages. He daily sees sick people, and this puts the senses on stretch to help, to learn, to understand. Cancer supplies the patients, and the patients supply the motivation. The endless manifestations of disease stimulate questions which are prelude to systematic inquiry. Thus, studies on mechanisms of anemia, increased energy metabolism, hypoalbuminemia, hypercalcemia, hyperuricemia, and other pathophysiological phenomena have had understanding to the tumor-host relationship and improvement in medical therapy (20, 42). Further these syndromes are common to diseases other than cancer, and investigation of their pathogenesis, consequences, and management has wide applicability in general medicine.

In other clinical studies it has been found that many human tumor cells of different cellular origin have acquired the capacity to elaborate substances which profoundly modify the host’s physiology (8, 9, 15, 32, 39, 41, 47, 58, 63, 71). Thus there are bronchogenic tumors which elaborate a polypeptide with adrenal corticotrophic activity, producing Cushing’s syndrome in the patient. There are patients with renal carcinomas, cerebellar he-
globulins or the smaller Bence Jones proteins; the pattern of a patient with multiple myeloma.

The chemical properties of the abnormal serum γ-globulins were previously obscure clinical manifestations of the disease. When serum proteins began to be studied, electrophoresis was difficult, so little was done with this new parameter of the disease. Then in 1951 Durrum described the technic of paper electrophoresis; it was quickly applied to the study of serum proteins in health and disease with an explosive expansion of knowledge about multiple myeloma. Skeletal manifestations of pain, pathological fracture, hypercalcemia, and bone marrow replacement were long thought to be the major characteristics of the disease. When serum proteins began to be studied, first by chemical separations and later by electrophoresis, it was recognized that there were quite specific changes in the γ-globulins. But the chemical procedures were not precise and Tiselius electrophoresis was difficult, so little was done with this new parameter of the disease. Then in 1951 Durrum described the technic of paper electrophoresis; it was quickly applied to the study of serum proteins in health and disease with an explosive expansion of knowledge about multiple myeloma and its interrelationship with other neoplastic and non-neoplastic diseases (29, 53).

Routinely applied, serum protein paper electrophoresis quickly revealed that myeloma is more common than previously recognized. Many of the previously obscure clinical manifestations of the disease can now be related to specific physicochemical properties of the abnormal serum γ-globulins or the smaller Bence Jones proteins produced by the neoplastic plasma cells.

In 1957, Dunn (12) and, contemporaneously, Rask-Nielsen (57) described spontaneous plasmacytomas in mice. These observations led to a study of the serum proteins in the tumor-bearing mice by Potter, Fahey, and Pilgrim (54), and there was the homogeneous γ-globulin spike resembling the pattern of a patient with multiple myeloma. More recently Potter (55) has demonstrated that the injection of Freund's adjuvants intraperitoneally in mice results in the production of a spectrum of plasma cell tumors. These tumors and their specific protein products, as well as the abnormal serum proteins in human multiple myeloma, are currently the subject of intensive biochemical and immunochemical study in a number of laboratories throughout the world.

We have traveled the road of cancer research, and I have pointed to sights that impressed me. In the journey, I am sure that you have seen many things which I overlooked. When we started this historical tour the central problem of cancer research was, "What is the nature of the neoplastic cell?" In 1963, we have a vastly richer dossier on the cancer cell than was available at the beginning of the century. Many of the queries have been answered: the base ratios of tumor cell DNA do not deviate from normal, the pathways of purine and pyrimidine biosynthesis are qualitatively the same in normal and neoplastic cells, there are no control failures in energy metabolism of tumors, the profile of enzymatic equipment is not characteristically different between tumor and normal cells, to mention but a few facts. In 1963, the central problem is, "What is the nature of the neoplastic cell?" But we are way ahead because we know so many things that the tumor cell is not. Are you, with me, optimists who proclaim that we live in the best of all possible worlds, or are you pessimists who fear that this is true?

It would be safe, and quite prudent, to conclude that the problem of cancer is complex and as mysterious as the phenomenon of life. I want to be safe, but I also want to state my conviction that we are in a more favorable position than ever before to ask the right questions about the nature of cancer. We know that the neoplastic transformation is an event of the cell. There is no necessary interaction between a complex host environment and the cell destined to become malignant to effect the transformation. We know that the change is heritable. Big steps have been taken in defining the action of genes in physical and chemical terms.

Relatively simple systems are now available to break down and analyze the steps in tumor genesis. Thus normal cells can be cultivated under defined conditions. The viral agents are one class of etiological agents which can transform cells in vitro. Since it has been established that one type of tumor virus can induce cancer in many different types of cells, it appears that results in this system would carry generality in their interpretation. Already much is known about the specific sequence
of biochemical events following virus infection of a cell, and these must be followed step by step in the neoplastic transformation.

The systems for studying the details of differentiation in precise chemical terms are being developed (6, 16, 44). This has applicability to the questions about cancer, for the controls which determine the balance between cell replication and non-replicative function must be clarified in the approach to understanding of cancer.

The contribution of research up to the present toward deepening the understanding of cancer is tremendous. Just as classical genetics was essential for defining the problems and presenting the issues most appropriate for study at the molecular level, so cancer research has brought the problem of the neoplastic cell to the point where the intimate differences between gene action of normal and of tumor cells can profitably be explored. "The end," said Emerson, "preexists in the means." I believe that the right means are now at hand for solution of the fundamental problem of cancer by systematic basic research.

This is a personal credo which I state firmly, even while recognizing that I may sound like the Victorian politician Lord John Russell about whom a contemporary wrote, "He would perform the operation for the stone, build St. Peters, or assume, with or without ten minutes' notice, the command of the Channel Fleet: and no one would assume, with or without ten minutes' notice, the command of the Channel Fleet: and no one would

Having stated my conviction regarding the possible characteristics of the road ahead, however, I would also like to comment on another pattern of investigation which has come into existence in recent years. I refer to the "organized" or "directed" health research program. This, historically, was created to evaluate penicillin in syphilis, streptomycin in tuberculosis, corticosteroids in rheumatic fever, and psychic energizers in mental disease. It uses personnel in many institutions who accumulate data according to a pre-determined plan and pool their results. In cancer the major organized program has been in chemotherapy, and for this and other directed research I can muster little enthusiasm (21).

There is ample precedence for emphasis on a particular technical field which comes from the interplay of contemporary events and science. The relevant example is the demand and aspiration of the American public for relief from the hazards and toll of disease, which has led to the Federal appropriation of vast sums for health research. Cancer has been high on the list; not only has the area been given money for research, but the appropriation has been further categorized into specific subject headings. Cancer chemotherapy has been favored.

This is understandable, but it has a built-in hazard which I believe we in cancer research have either been slow in recognizing or cavalier in disregarding. This is that the amelioration of cancer cannot be achieved by the overemphasis of target work out of all proportion to its possibility of realization. The frontal assault on cancer has been fostered by appeals to the public with the assurance that the fastest way to conquer cancer is to donate dollars, by publicity which spectacularizes and overinterprets minor gains, and by representations to Congressional Committees which emphasize the possibility of the direct short route to the answer rather than the probability of the long, circuitous, and unpredictable path of fundamental research.

It has been said that no individual research of merit has been deprived of funds because of their diversion to organized programs. I am sure that this is so, but my concern continues and is based on the following considerations:

a) Disillusionment of the laity with science and scientists because success has not been bought with dollars, contrary to expectation.

b) Recruitment to the ranks of laboratory and clinical cancer research of potentially capable investigators who will either become bored and discouraged by repetitive data accumulation and leave the field or, equally unfortunate, remain and perpetuate a low-yield system of study.

c) The discouragement of young men and women from becoming identified with cancer research for fear that the area is too categorical and narrow.

d) The dilution of efforts of those whose time could be spent more profitably in productive investigation.

The records of our accomplishments support the view that there remains the necessity as far as our vision now extends for emphasis on individual rather than collective research and for the support of individual creativity rather than collective ideation. I remind you that these views on planned research are personal and are not entirely shared by many better qualified colleagues.

We have considered the place of cancer research in science and we have mentioned the pressures generated by contemporary history which impinge upon and in part mold cancer research. Now I would like to discuss the current climate of science in society. The structure of research as we know it today (61) is built to the extent of between 50 and
60 per cent upon governmental financial aid. Of the remainder, 30 per cent is supplied by industry, largely for its own programs, and 10–15 per cent comes from philanthropy, endowment, state governments and other non-Federal sources. The administration of Federal grants through participation of non-governmental scientists in the Study Section System, implemented by devoted, skilled, and sympathetic officials of the National Institutes of Health, has been a model of effective support for scientific advance through research. This happy state of affairs received a preceplible jolt at the end of 1962 with the issuance of a new Grants Manual from the National Institutes of Health (70). This Manual supersedes the administrative guide of 1959 (69).

There are in the new Manual a number of changes which can best be classed as Petty Nuisances with Potentialities for Growth or as falling within the Department of Fancy and Speculation. In the former are the new regulations regarding Equipment (Section 541B1). These state that equipment may be purchased after an appropriate administrative official of the Grantee Institution determines that no other equipment is available or suitable for the purpose. This provision evokes the picture of a grantee with two Beckmans in boxes and another half dozen on order against a rainy day; or some other type of injudicious, indefensible, incredible incursions of the proper use of the grant money for equipment. The question is, how often has this occurred? Aside, however, from the implication that all grantees carelessly and unnecessarily duplicate equipment easily available to them, is this more than a nuisance item to the grant recipient? At the moment, probably it is not; tomorrow or the day after, depending upon administrative actions which might be taken at either the Federal or the local institutional level, this apparently innocuous regulation could effectively hamper research.

Later in this same section of the new Manual it is stated that grant funds may not be used for the purchase of any equipment costing in excess of $1,000 which has not received prior Public Health Service approval. Again it is clear that a reasonable and rapid decision would be made on such requests by the administrative personnel now serving at the National Institutes of Health. The note of mistrust which has been added in the relationship between grantor and grantee is, however, distressing and suggests that the NIH doesn’t know whether the recipient is reliable or reprehensible. It naturally leads the grantee to consideration of what would happen if the NIH official were wicked, not wise.

In the category of the fanciful, I would place Section 541B2, Estimates of Effort. It says that Quarterly Effort Reports shall be made on all professional staff receiving salary in whole or in part from a Public Health Service Grant. Reports, expressed in per cent, it continues, shall reflect estimates of the effort expended by the salaried person on each grant for which salary is being paid. The percentage effort must equal or surpass that agreed upon in the application and award. This lends itself to the venting of pent-up exasperation with administrative lunacy, as in one Effort Report that I saw in which a salaried professional was recorded to have expended 13.672 per cent effort, the calculated proportion of his total salary received from the grant. Obviously, however, the Estimates of Effort can be highly destructive. If you are training a fellow in research, is this an effort on the research grant? Should those of us receiving salary support from USPHS Grants consider the time at this scientific meeting as effort on the grant? If I had the decision to make I would certainly allow you effort and a half for this session. At best this requirement cannot be honestly met, and it potentially opens the way for administrative abuse.

Much more critical and serious than these details are the sections of the Grants Manual which indicate a new attitude toward scientific investigators. Section 502 deals with the purpose of the research grants. In essence it states that the grants “are intended a) to expand research activities throughout the country, and b) to encourage investigators and institutions to undertake research in relatively neglected scientific areas.” It is, in fact, a verbatim replication of the statement in the 1959 Manual with the exception that the last sentence of the paragraph in the 1959 document has been omitted from the 1963 edition. It read, “In carrying out these objectives, the aim of the Public Health Service is to promote the highest quality of research without interference or control.”

Before attempting to assess the implication of this omission, attention is called to Section 525, 1963 Manual, entitled “Scientific Freedom—Change in Project.” It states, “Subject to such restrictions as the Surgeon General may prescribe, the investigator may make changes in methodology, approach or other aspects of the project, which in his judgment, would expedite achievement of the research objectives of the project; however, no change may be made which would constitute a significant deviation from the nature and purpose of the approved project or which would impair the achievement of the purpose for which the project was approved.” This is an am-
biguous statement, for “restrictions which the Surgeon General may impose” are not defined nor is it indicated who is to judge whether a “significant deviation from the approved nature and purpose” has occurred or whether the deviation “would impair the achievement” of the goal to be achieved. Contrast this section with the comparable one in the 1959 Manual: “Every effort is made to protect the scientific and academic freedom of the principal investigator. Although he submits a proposal for review as indicated in the preceding section, he is free to pursue the project in whatever manner he deems most promising.”

I have no hesitation in stating that these two comparisons alone demonstrate a change in attitude toward the investigator which constitutes a clear and present danger to scientific research.

An analysis of the immediate events which led to the new policy indicates that the NIH has responded to pressure from a subcommittee of the House Committee on Government Operations (35, 36, 64, 65). The Intergovernmental Relations Subcommittee chaired by Mr. L. H. Fountain has investigated the administration of grants by the NIH during the past four years. On the basis of finding a number of irregularities in an unspecified number of grants (only one is explicitly discussed in the public records of the hearings), the Fountain Committee castigated the NIH for laxity in its administration. Some years ago the Ford Foundation was characterized as a large body of money completely surrounded by people who want some. This seems to be the attitude of the Fountain Committee toward the NIH and the scientific community. In hearings before the Committee in 1961 and 1962, the NIH and particularly its Director, Dr. James Shannon, gave eloquent and carefully reasoned testimony on the importance of freedom to research, on the achievements of the system which selected investigators on the basis of scientific merit, and on the encouragement of creative research. The fallacy of generalizing from individual cases of grant money misuse in an operation which has more than 15,000 grant awards was emphasized, but to no avail. A subsequent report of the Fountain Committee to the Congress ended with the words, “The conclusion is inescapable, from a study of NIH’s loose administrative practices, that the pressure for spending increasingly large appropriations has kept NIH from giving adequate attention to basic management problems. The Committee expects NIH to give high priority at this time to the task of correcting the management deficiencies and strengthening its capacity for the effective and efficient operation of these vital health programs.”

The new Grants Manual is the result, and you are hereby demoted from scientists to “Management Problems.”

That which has come to pass is serious, but it is by no means overwhelming. The Grants Manual just issued indicates clearly that we should analyze the basis for the changing climate and attempt to proceed rationally. Only if we withdraw into haughty disdain or, alternatively, fawn submissively will policy be established without relation to the needs of science.

Many explanations have been suggested for the apparent fall from grace. These include the proposition that there has been too rapid growth of research support, and this automatically is subject to Congressional question; the presumption that some documented irregularities in the use of research money reflect a general pattern; that scientists collectively are becoming an arrogant class of “Herrenvolk” and they need to be humbled, etc. All these and others undoubtedly are factors, but I wonder if the major problem is not one of communication. Our representatives in Congress apparently believe that business procedures and elaborate bookkeeping will make scientific research more efficient; this is as confused as Samuel Butler’s sly suggestion that the hen is the egg’s way of making more eggs. We have failed to make known what our work is and why it is important that it be accorded freedom to proceed without restrictive regulations. It must be made clear by each one of us in our day-to-day communications with the public and by articulate spokesmen to governmental bodies that research is a continuing formulation of questions. The answers obtained determine the next questions asked. A program which can be precisely planned and budgeted in detail a year in advance is not a research undertaking, it is a duplication-of-data activity. Research, which potentially may enlarge understanding, will falter if fettered. Dr. Shannon makes the point succinctly, “Freedom of the investigator is not something valuable or useful in itself. It has been proved to be effective in bringing forth research findings. Freedom is defended not on abstract grounds or as an inherent right of scientists, but as the prime condition for assuring maximum yield on the taxpayer’s investment in medical research” (65, p. 15).

I am confident that a real withdrawal of public support from research will not occur. The interdependence of society and science is too well established. Individually and collectively we must effectively take the steps to hear and be heard on questions of the purpose of science and science administration and thus maintain the conditions...
necessary for work. Be sustained in this by the words of Thomas Paine, "Those who expect to reap the blessings of freedom must, like men, undergo the fatigue of supporting it."

And now in closing, I would like to explain the title of this talk. In 1960 in Israel leaders of the new nations in Africa and Asia came to an international meeting with scientists from all over the world. There, Abba Eban said, "The fabric of history has a single unifying thread—a constant direction of human history, in the responsiveness of men when challenged by great issues and lofty ideas."

Cancer research is a response to a great issue in human health. The fruit of our efforts, when successful, will not be the prevention of death but the enrichment of life. As a part of all science and therefore also a part of the thread of human history we are fortunate in being able to devote effort and sympathetic concern to the expanding welfare of mankind.

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The Unifying Thread

Alfred Gellhorn


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