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Collaboration for Accelerating Progress in Medical Research

Albert B. Sabin

Fully recognizing the importance of assuring that the laboriously acquired existing knowledge not remain on library shelves to be admired like great works of art in museums but be expeditiously put to work for human welfare, I nevertheless wish to limit my present statement to the problems involved in the acquisition of the new knowledge that is needed for the elimination or alleviation of human disease and for the improvement of human health.

Let me first of all agree with those who stress the importance of the individual scientist's search for knowledge for its own sake as the very foundation of scientific endeavor that must continue to be supported *and expanded* if science is to provide the means for the solution of the many problems of importance to human welfare. Unlike many other types of scientific research, medical research is by its very nature oriented toward specific goals directly related to human health. As I see it, the real issue in medical research is not so much the maintaining of a proper balance between so-called basic research, designed chiefly to provide understanding of life processes, and so-called applied or mission-oriented research, designed to achieve a well-defined objective like the prevention, alleviation, or cure of a disease—because to achieve the latter you must invariably also engage in the former—as it is the proper definition of important specific targets that call for and are ready for a concentrated, well-planned, and coordinated research effort. As more and more people enter the field of medical research and more and more money becomes available for it, there is unfortunately an increasing proportion of persons who choose to work on little problems that they can handle by themselves or in collaboration with small groups of junior investigators. The important issue, it seems to me, is whether enough is being done to develop *acceptable* mechanisms for coordinated and cooperative research—regardless of whether it be for achieving the initial basic understanding or the ultimate control of a disease—to attack those larger and more complex problems whose solution can be markedly retarded if the necessary work is left to the chance interests and uncoordinated efforts of the individual scientists. My own conclusion is that much more needs to be done than is now being done, and in what follows I examine the question of whose responsibility it is to plan for a more concentrated attack on the more complex disease problems, and to consider new mechanisms for planning, for establishing priorities for funding—because money for research, like money for everything else, must be budgeted—and for implementing the decisions that are reached. The decisions that I have in mind would have to be made by the most competent scientists, who will have to do the work; by the administrators, in conjunction with their advisory councils, who will have to establish priorities on the basis of relative importance and need; and by the Congress representing the public, from whom the money will have to come for translating reasonable plans into working projects.

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Responsibilities and Opportunities

To begin with, I should like to say that in my judgment there is a need for additional attention by federal agencies in the field of biomedical development, particularly for establishing suitable procedures for planning and implementing the type of collaborative research that I have just mentioned. Various professional societies, including the Division of Medical Sciences of the National Research Council, as well as federal agencies such as the National Institutes of Health and the Armed Forces Epidemiological Board, often arrange symposia or special study groups to emphasize or identify research needs relating to certain diseases or health problems, and these are useful in calling the attention of the scientific community to important fields of research that are either neglected or receiving insufficient attention. With relatively few exceptions, however, the implementation of these needs is left to chance—the chance that individual scientists will develop an interest and come up with suitable programs. I believe that certain federal agencies, particularly the National Institutes of Health, through the intramural programs of their disease-oriented Institutes and their function as transmitter of public funds for the support of extramural research, have both special opportunities and special responsibilities for assuming the leadership for planning and implementing research on the complex problems that are not now receiving sufficient or adequate attention through the efforts of individual scientists.

Present Procedures

In my judgment, existing procedures for the establishment of long-range plans and priorities and for their implementation are not commensurate with the needs. Lest I be misunderstood, I want to say to begin with that the National Institutes of Health of the United States, justifiably envied throughout the world, constitute one of this country's finest national resources. The methods used in the past, under the exceedingly able leadership of the present director, James A. Shannon, have contributed to an extraordinary growth in medical research capability in this country. The procedures used in the past for evaluating the research activities of individual investigators through the agency of expert study sections is still the best that has been devised. There is, however, one legal provision which, in my judgment, has not only outlived its usefulness but is actually hampering the fulfillment of the missions for which the institutes were established. I refer to the legal requirement that the National Advisory Councils must approve applications for research grants, already carefully evaluated by the specialized study sections, before payment can be made. The National Advisory Councils lack the competence of the study sections; moreover, the extraordinarily large number of applications in recent years makes it virtually impossible for the councils to look at more than a few applications, and with only rare exceptions the recommendations of the study sections are confirmed. Yet most of the time at the three annual meetings of the National Advisory Councils, preceded by many hours of homework, is usually taken up with consideration of individual applications, to the exclusion of the more important functions of advising on the optimum utilization of funds by assigning priorities to the different spheres of activity falling within the mission of the institute, or of evaluating the overall planning of the activities of the institute. I frankly do not regard my own present service on the Advisory Council of the National Institute for Allergy and Infectious Diseases as fulfilling any useful function. I strongly recommend that the present Act be amended to remove the requirement of approval of individual research grants by the National Advisory Councils. I would hope that this would free these councils for another type of activity, in which their judgment can be used in evaluating plans for collaborative research and in assigning priorities to the various projects that are proposed.

In his testimony before the Senate Subcommittee on Government Research (Senator F. R. Harris, chairman) on 1 March, Shannon also expressed the opinion that the activities of the Institute councils in reviewing individual grant applications for so-called program relevance are now less feasible, as well as less meaningful than they formerly were, and stated that "it has been possible to shift the emphasis of Council activity to the broad consideration of program planning and evaluation." As far as the council on which I am serving is concerned, this still remains a desirable achievement for the future. Shannon also stressed that "the planning process must be centered in the fulltime activity of the staff of an Institute," but that, "given this, there then emerges a special role for the Council and for special disease- and problem-oriented committees." He stated that such special planning committees, "with membership drawn from outstanding experts in relevant areas," are now in the process of "being set up throughout NIH programs," and that "each Institute may have as many of these committees as are needed to cover its major disease or disciplinary concerns." He further stated that "committee responsibility for its assigned area includes examining and reporting on 'the state of the art,' and identifying gaps in present support as well as areas warranting increased program attention."

Although a few such activities have been in existence for a number of years in several institutes—for example, the chemotherapy and leukemia contract programs of the National Cancer Institute and the Collaborative Contract Program for development of certain vaccines and for studies on the immunology of organ transplantation of the National Institute of Allergy and Infectious Diseases—the establishment of "disease or specific problem-oriented committees" at the National Institutes of Health is still largely a matter for future accomplishment. Moreover, if the main function of such committees is only to identify gaps in present activities, as indicated by Shannon, without new plans being proposed for implementing the committee recommendations and for establishing priorities for carrying through the recommendations, I fear that very little progress will be made. Existing contract programs, under control of full-time Institute staffs and not subject to evaluation by the Institute Advisory Councils, have come under considerable criticism for the type of research programs they have contracted for, for the frequently poor caliber of contractors, for insufficient participation of the working scientists in developing cooperative research plans, and for being only another form of especially costly, individual-project-type research without the usual evaluation of study sections and without the necessary ingredients of a coordinated plan of attack.

Proposed Supplementary Procedures

I concur in the view that it is desirable to establish, as soon as possible, as many of these "disease or specific problem-oriented committees" as each Institute may require to cover the various fields within its mission, and I would like to propose some specific procedures for the operation of these committees and to suggest what should be done with their recommendations to permit optimum implementation and the greatest benefit for the solution of important problems. Briefly, my proposals are as follows:

1) Each Institute director, aided by his full-time staff, and with the advice of the chairmen of the Institute study sections and of the Advisory Councils for the intramural and extramural programs, shall draw up a list of important disease problems for evaluation of current activities, not only within the framework of the intramural and extramural programs of the Institute but within that of the country and world at large, and for decision as to whether or not programs could be accelerated through a cooperative and coordinated effort in the light of available technology.

2) The ad hoc committees charged with evaluation of a specific problem shall be made up predominantly of people currently working in the field, and shall include only an occasional "elder statesman" with past experience in the field.

3) If a committee decided that, in the present "state of the art," very little if anything could be gained from a collaborative, coordinated program, its immediate assignment would be finished, until such time as new developments might justify its reactivation. If however, the committee decided that there are important gaps in our knowledge which could best be filled through a coordinated, cooperative effort, it should then be charged with drawing up the research plan and providing an estimate of manpower needs and cost. If money were no object, the committee could then be charged with implementing its program through recruitment of participating investigators and other measures—but, as we know only too well, money is not now available for everything that reasonable people believe should be done for the benefit of mankind. Therefore, there must be some system for establishing priorities not only within each Institute but also for all the Institutes, so that the people of this country and their representatives in Congress can be apprised of specific health research needs, their relative importance, their cost, and what could be bought with funds that might be appropriated in the light of all sorts of other needs.

4) Accordingly I propose that Institute directors, acting with the advice of their National Advisory Councils, assign priorities to the various programs submitted by the special committees, on the basis of relative importance and the best possible judgment of the possibility of obtaining an answer. These special programs, with their Institute-assigned priorities, should then be submitted to the director of the National Institutes of Health, who, with the help of his advisory committee, would then have the task of preparing another priority list in the light of the relative importance of the various proposed programs for total needs of specific health-oriented research. Only when this stage is reached should the matter be taken to the Congress. In my judgment the Congress and the public should be informed of all the collaborative programs that have passed through the fire of critical judgment. Any appropriations that Congress would be able to make would then be made on the basis of carefully thought out priorities rather than on the basis of the effectiveness of special pleaders for some special program. Moreover, insofar as Congress fails to find the money for many of the needed programs, the people will at least know what they cannot get unless they are prepared to spend more money.

This is also a good place to state my conviction that, if the people of the United States want to accelerate progress in specific health-oriented research, the Congress will have to appropriate special funds for these programs, because only a fraction of the total need could be met by funds available in current budgets for specific disease-oriented research projects. It goes without saying that the people who will have to carry out the work on the approved programs will come not from some reserve pool of manpower in outer space but from among those already engaged in individual research projects, supplemented by new recruits from the current training programs. Accordingly, it seems to me that congressional appropriation committees will be justified in asking the extent to which the cost of the new collaborative programs will be covered by items in the present Institute budget, and the Institutes will have to keep this in mind in preparing their regular as well as their special-program budgets.

5) The success or failure of collaborative, coordinated research programs ultimately will depend on the willingness of scientists to participate in such programs, and this in turn will depend on the extent to which they can participate in the original planning and critique of the total research plan and on the extent to which opportunities for individual initiative and ingenuity remain in the cooperative enterprise. This may turn out to be a much more formidable obstacle to the success of collaborative, coordinated programs than getting the money from Congress—unless the working scientists can be properly motivated and given ample opportunities for participation in development of the total research plan and ample opportunities for individual initiative in pursuing identified objectives, and unless they are properly rewarded with money and academic appreciation for what they are doing.

Many congressional and other special committees have done a good job of analyzing the workings of the medical research establishment, both within and through the National Institutes of Health, and all recommendations have stressed the need for more planning and for more so-called "directed research" (that is, goal-oriented or programmed); some have even suggested the need for a special breed of full-time executive, the "super" program manager. I submit that nothing could be more prejudicial, for obtaining the cooperation of American scientists in urgently needed collaborative and coordinated research programs, than use of the term *directed research* by either the Congress or the National Institutes of Health administrators. What is even more important than the name, however, is the manner in which such programs will be managed. In my judgment the original working-scientists committee whose plan for a special program has been adopted and funded should have the major responsibility for management of the program—for assignment of funds to participants; selection of participants and new recruits for the program; actual recruitment,

with various powers to entice co-workers; frequent discussion of results in progress; and cooperative modification of the total research plan as new situations arise. Each such group would require not only a tactful chairman from among the working participants but also a full-time executive officer from the Institute that would be responsible for funding and monitoring the program.

These are some ideas for *supplementing*, not replacing (I stress *not replacing*), the present procedures for supporting medical research in this country through collaborative and coordinated research programs for accelerating the solution of those problems that are too complex to be solved through the uncoordinated efforts of individual investigators.

Project Hindsight

A Defense Department study of the utility of research.

Chalmers W. Sherwin and Raymond S. Isenson

No matter how much science and technology may add to the quality of life, no matter how brilliant and meritorious are its practitioners, and no matter how many individual results that have been of social and economic significance are pointed to with pride, the fact remains that public support of the overall enterprise on the present scale eventually demands satisfactory economic measures of benefit. The question is not whether such measures should be made, it is only how to make them.

We wish to report here on an attempt by the Department of Defense to make such measures. This effort, known as Project Hindsight, is a study of the role that research played in the development of weapon systems between the end of World War II and about 1962 (*1*).

To appreciate the need for Project Hindsight one has merely to examine the budget of the Defense Department. In recent years, the Department has been spending $300 to $400 million a year for "research." Of this sum, we estimate that about 25 percent is committed to basic or undirected science, although concentrated in areas generally relevant to the DOD missions, and about 75 percent to applied science more directly related to defined DOD needs. The Department has been spending an additional billion dollars a year for "exploratory development," which includes the more sharply defined applied research, small-component development, and other activities of the sort generally characterized as "technology" (*2*). (This $1.4-billion expenditure does not include the system development programs which are its main reason for existence.) Questions were constantly being asked, both in the Executive Branch of Government and in Congress: Was this large a sum really needed? What has been the return for the expenditure? Can the Defense Department not depend for more of its science and technology on the private sector or on other Government agencies? These are reasonable questions, but there seemed to be no systematic, quantitative answers. One of the objects of Project Hindsight was to try to provide such answers; that is, to try to measure the payoff to Defense of its own investments in science and technology. A second object was to see whether there were some patterns of management that led more frequently than others to usable results and that might therefore suggest ways in which the management of research could be improved. In particular, we wanted to determine the relative contributions of the defense and non-defense sectors, and, within the defense sector, the relative contributions of in-house laboratories and those of contractors.

Assumptions and Methods

Given these objects, how does one start? Since the challenge was essentially an economic one, the answers would have to be based upon economic benefits. The economic return of a scientific or technical innovation is through its utilization in an end-item—a piece of equipment, a process, or an operational procedure. Therefore in order to assess return one has to measure the value of the end-item made possible by the innovation. As a practical matter, for military hardware the easiest way of measuring economic benefit is by comparing the value of an end-item with that of some predecessor end-item which it partly or wholly replaces.

Our method of analysis was as follows: One begins by comparing a successor item with a predecessor, identifying all the contributions from science and technology which were significant in the improvement in performance or the reduction in cost of the item. One then estimates the portion of the increase in the cost-benefit of the end-item which is attributable to the scientific and technical innovations utilized. (This portion is, of course, very large for defense equipment.) One then calculates what it would cost to obtain enough predecessor equipment to do the job that the successor equipment is now doing, assuming that the same capital resources and management skills were available for the predecessor as for the successor. The difference between this cost and the actual cost of the successor is a measure of the economic benefit assignable to the set of significant contributions from science and technology which were utilized in the successor

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