14 December 1956, Volume 124, Number 3233 SCIENCE

Medical Research in Perspective

James A. Shannon and Charles V. Kidd

The years since World War II have witnessed a many-faceted revolution in medical research in this country. Perhaps the most significant aspects of this revolution relate to the substance of medical science itself, to such things as the unprecedented and enormously fruitful adaptation of the techniques of the physical sciences to biology and medicine. There have been, however, equally interesting developments relating to the means by which scientific ends have been achieved. Some of these developments, which have a profound but often unrecognized impact on progress in research, are the subject of this article. We wish to discuss changes in the volume and source of funds for medical research and some of the implications of these changes. Then, in particular, we discuss the manner in which support of research by the U.S. Public Health Service through the National Institutes of Health affects institutions and individuals.

Volume and Sources of Support

The dollar volume of support for medical research in this country has increased from some $40 million to some $240 million over the past 15 years (Fig. 1). This is rapid growth, but two pertinent facts should be borne in mind in considering the rate of increase. First, it has simply paralleled the increase for all research and development in the United States over the same period, continuing to represent roughly 5 percent of that total. Second, taking into account the decline in the value of the dollar, the $240 million represents only about $120 million in 1940 dollars, or a threefold expansion of effort as measured in dollars of constant purchasing power.

In all probability, these data understate the increase in support for medical research during this period. There are no fully reliable estimates of expenditures for medical research for the years before World War II, but the estimate of 1940 expenditures is probably somewhat high.

Accompanying this marked change in the total dollar support of medical research are changes in the origin of the dollars (Fig. 2). In the immediate prewar period, 1940, the federal contribution to the national support of medical research was some $3 million, representing 7 percent of the total. By 1944, in the latter part of the war, expenditures for research and development for the conduct of target research by the Armed Forces and by the Office of Scientific Research and Development increased the federal expenditures to $10 million, representing about 16 percent of the total. The year 1947 may be considered the first year of the postwar era in medical research. Support by the Federal Government expanded markedly to a level of $28 million in absolute terms. In addition, the proportion of all expenditures represented by federal funds was 32 percent, twice the 1944 proportion. By 1955 the total support of medical research had risen to $240 million, with the Federal Government's share being $113 million, or more than 40 percent.

During the years since World War II, the large volunteer health agencies have greatly expanded their support of medical research, while the relative—but not the absolute—contribution of the older endowed foundations has declined. It is very significant that the increases in Government support have not reduced the contributions from philanthropy, endowment, or private industry. In fact, private support for medical research has increased in the postwar period, although not in proportion to the expansion of federal aid.

Sites of Research

Not only the source and volume of support for the national medical research effort, but the location of the research is important. Somewhat more than $40 out of every $100 for medical research is expended in medical schools and universities. In absolute terms, these institutions spent about $100 million in 1955 for medical research (Fig. 3). Roughly $75 million of this total was spent in medical schools.

One of the most significant aspects of the financing of medical research in academic environments is the diversity of sources of support. Less than $20 million of the total of about $100 million expended in these institutions came from endowment, or "hard money." About $30 million came from all kinds of philanthropy—individuals' gifts, private health associations, and foundations. The contribution directly from industry was small, but the indirect industrial contributions (typified by such groups as the industry-supported Life Insurance Medical Research Fund) counted as philanthropy were substantially larger. Finally, the Federal Government provided $55 million to these laboratories in 1955. It is abundantly evident from these figures that academic research is largely dependent on sources of support which are not controlled by the institutions themselves. It seems quite probable that endowment income will not rise to a level that will change this situation in the foreseeable future. Moreover, one may question whether support from private philanthropy will rise markedly. Hence, there is a high probability that the two major sources of expanded support for medical research in the future will be corporate giving and federal funds.

In addition to the medical research

Dr. Shannon is director of the National Institutes of Health, U.S. Public Health Service. Mr. Kidd is chief of the Office of Research Planning, National Institutes of Health. This article is based on a paper presented at the annual meeting of the Division of Medical Sciences, National Research Council, Washington, D.C., May 1956.

conducted in private, nonprofit institutions, medical research conducted by pharmaceutical firms and other industrial concerns approximated $80 million in 1955. Much of this work relates to process research, product development, and associated lines of investigation, but substantial sums are spent for more general studies.

Finally, the medical research laboratories of the Federal Government had current operating budgets of about $58 million in 1955.

In view of the national significance of federal expenditures for medical research, these funds and the policies that govern their distribution deserve careful attention.

Federal Expenditures for Medical Research

The total federal expenditure of $113 million for medical research in 1955 was made through five administrative agencies—the Department of Health, Education, and Welfare ($64 million); Department of Defense ($31 million); Atomic Energy Commission ($11 million); Veterans Administration ($6 million); and National Science Foundation ($1 million) (Fig. 4).

One might question—and many have—whether support of medical research by five different federal agencies is a sound way to conduct the affairs of government. The obvious objections to such a system are that duplication of administrative effort may be involved, that lack of coordination is possible, and that duplication and overlapping of research support can occur. In practice, these have remained potentialities. On the other hand, in research, as contrasted with most other activities of the Federal Government, a positive and fundamental advantage arises from performance of roughly the same function by several agencies. Diversity of sources of federal support is important because the most significant decisions relating to support

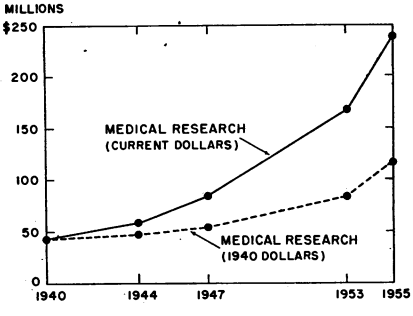

Fig. 1. Expansion of medical research in the United States, 1940–1955, in terms of current cost (estimated) and 1940 purchasing power.

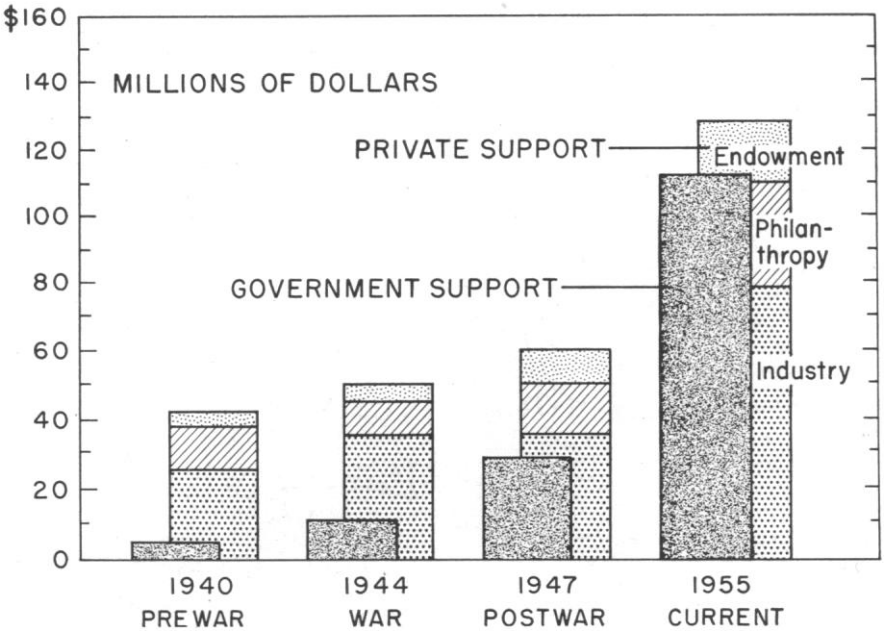

Fig. 2. Cost of the nation's medical research in four key periods, showing sources of support.

of medical research are matters of judgment. When scientific judgments are involved, the total research program of the nation is best served if decisions are not centralized but dispersed so that various advisers, various points of view, and various interests can be brought to bear on complex problems. And from the standpoint of those whose research is supported by federal funds, there are dangers in having all the "eggs in one basket." Neatness, symmetry and simplicity, which might appear in the organizational chart if a single agency were responsible for research support by the Federal Government, would not contribute to the essential efficiency and productivity of the federal effort.

The amount of federal funds for medical research is now so large that not only the volume of funds but the terms and conditions for receipt of funds are matters of high significance to the total medical research program of this country. Just why this is true can be seen by looking in some detail at the questions of policy that have arisen in connection with the research grants and training awards administered by the National Institutes of Health.

Budget of the National Institutes of Health

Take first the magnitude of the budget of the National Institutes of Health. Figure 5 represents the development of the program over a 10-year period, broken down into (i) direct operations and (ii) research grants and training. For the year that ended 30 June 1956, the total budget of the National Institutes of Health was $98 million (Fig. 6). Of this, approximately $30 million was expended for the operation of the NIH laboratories in Bethesda, Maryland, and elsewhere. The great bulk of the remaining $68 million was distributed to medical schools, universities, hospitals, and other nonprofit research institutions.

For the year beginning 1 July 1956 (federal fiscal year 1957), the appropriation for NIH will total $183 million. The direct research funds will rise from the $30 million of the preceding year to $37 million. This increase will be used almost entirely to complete the execution of a 10-year plan for full utilization of the Clinical Center, a large new building for laboratory-clinical investigation.

The funds for research grants, for training, and for some relatively small related programs will be at a level of $146 million, an increase of $78 million over the previous year. It is worth noting that of the total increase of $85 million, $78 million is for grants and awards as compared with $7 million for the direct federal operation.

The large increase in grant funds is, in effect, a statement of national policy by Congress that lack of funds should not impede medical research in this country. The appropriation, however, is viewed not as a blank check to be used as a subsidy for any research or training proposals that may be made. Rather, it is viewed as an unparalleled opportunity to move the medical and biological aspects of research in this country ahead as rapidly and as productively as possible,

with maximum utilization of existing facilities and of the present supply of qualified investigators, and with particular attention to strengthening the research potential in years to come. In some fields, the funds provided by Congress will undoubtedly prove to be more than can be effectively expended. In this connection, discussions with the numerous scientific advisers to the various institutes have revealed a spontaneous consensus to the effect that the standards of eligibility for receipt of any grants from NIH should not be relaxed in any way.

Viewed in this light, the 1957 appropriation for NIH does not modify the basic objectives of the programs—the support of medical research and training for research throughout the country—nor does it solve continuing policy questions involved in the administration of these Public Health Service programs.

Categorical Approach

Research grants from the NIH are distributed through a series of institutes that bear the names of categories of disease—cancer, heart disease, and so on (Fig. 7). Support of research through an organization based on categories of disease has certain inherent potential problems, such as the obvious one that orientation toward certain diseases will lead to pressure for quick production of applicable findings, thereby sacrificing basic research.

A primary aim of the NIH is to administer the programs in a way that prevents the potential hazards of the disease-category system from becoming real.

It should be noted that there is nothing in the disease-category approach to medical research that is inherently less desirable than, say, an approach based on organization according to scientific disciplines, or one based on body organs or systems. What is required is that any system of categories include the total range of relevant inquiry and that relevance be intelligently defined. This is the case with respect to the totality of the disease categories that describe the missions of the seven institutes comprising the NIH. It is certainly true that any system of fragmenting knowledge in order to organize thought and work can lead to isolation of areas of thought and to sterility of thought within the confines of a narrow category. In any case, common usage rather than logic confines the meaning of categorical research in medicine to the category defined in terms of groups of diseases. Support of research in categories defined as scientific disciplines would represent the same potential danger to the prosecution of fully effective research as does the defining of categories by disease. This point was epitomized by Detlev W. Bronk when he said, "Why is it that a person who studies the heart action of a frog is a zoologist while one who studies the heart action of man is a physiologist?"

Moreover, the potential relevance of research to any disease category is defined in terms of long-range possibilities and not in terms of work directed toward the quick solution of problems obviously and solely related to a given disease. These two factors taken together permit support of research of the type that the scientific world takes for granted as the essential prerequisite to large forward advances against specific diseases. It is significant that this view is shared and formally stated by Congress. For example, in June of this year the Senate Appropriations Committee submitted a report to the Senate containing these words: "The Committee reiterates the fact, expressed in its reports of earlier years, that it positively encourages the use of cancer research funds, and funds of other Institutes, for fundamental studies—such as steroid chemistry and cell physiology—which must underlie clinical and laboratory investigations directly related to specific diseases" (*1*).

Investigators throughout the country are for the most part, but not entirely, convinced that they need not "angle" what they wish to do in order to increase the probability of receiving a research grant from the NIH.

Ultimately, the disease-category structure for research support by the NIH is a consequence of the interests and desires of the American people, reflected in the actions of Congress. Increased popular support of medical research is predicated on public confidence that research will yield answers to problems of disease.

The goal sought is not a scientific but a moral one. Congress, on the national scene, interprets the moral end in the political terms required if the urge to help relieve pain and prevent death is to be more than an aspiration. This interpretation, which is in effect the construction of a bridge between widely shared humanitarian goals and the world of research within which these goals are sought, relies upon disease categories. People understand disease, and research can be productively segmented by disease category with the application of intelligence, common sense, and due concern for the essential unity and increasing interdependence of the scientific disciplines.

Project System of Support

The NIH programs are characterized not only by a disease category form of organization, but by a project system of support. The research-project approach can be pernicious if it is administered so that it produces certain specific end products, or if it provides short periods of support without assuring continuity, or if it applies overt or indirect pressure on the investigator to shift his interests to narrowly defined work set by the source of money, or if it imposes financial and scientific accounting in unreasonable detail.

After 10 years of experience in the administration of a system using the word "project" for the applications sub-

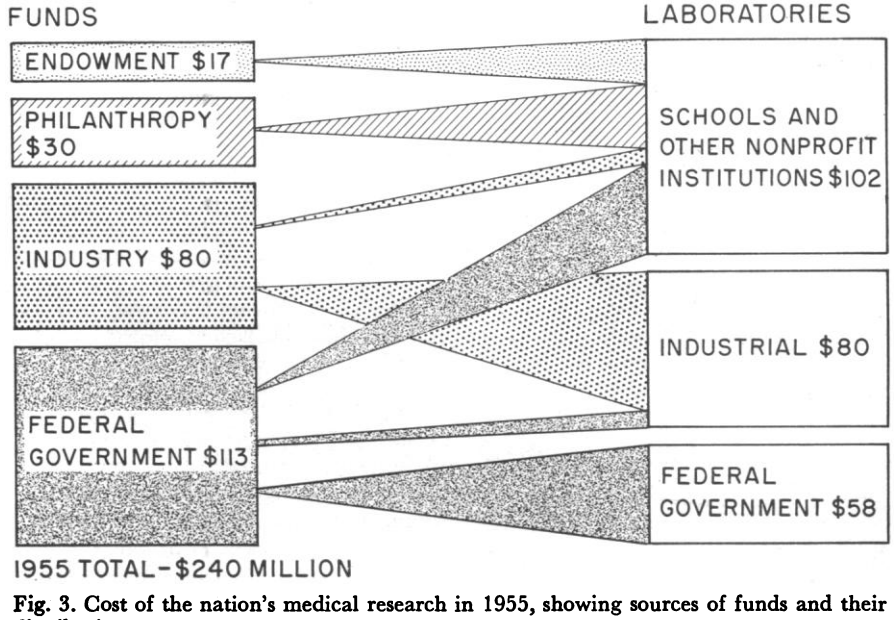

Fig. 3. Cost of the nation's medical research in 1955, showing sources of funds and their distribution.

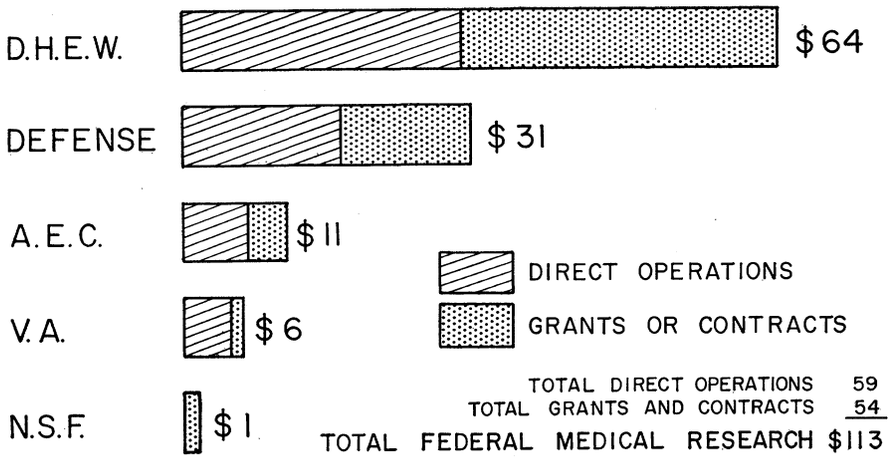

Fig. 4. Total federal expenditure (millions of dollars) for medical research in 1955, by agency and type of program.

mitted by investigators, it appears that the evils noted in the previous paragraph can be and have been averted, primarily by attention to procedures centering around extension of the freedom of the investigator.

Freedom is extended by quite specific principles, devices, and actions—for example, by providing more funds for broadly defined areas of study and more support for research that is not directly related to a specific disease; by increasingly stable support; by freedom to change lines of inquiry; by freedom to shift the uses of budgeted funds; and by freedom from detailed reporting requirements.

The degree to which such basic objectives are attained is an important criterion used by the NIH and its advisers in assessing the quality of administration of the program of research grants. The fact that, by statute, support can be provided only for research described as a project is a matter of minor consequence as compared with the more basic characteristics of the program.

Thus, both the categorical approach and the project system are viewed by the NIH and its advisers not as fundamental characteristics of the grant programs but as relatively superficial operating methods. The fundamental matters relate to the specific operating policies designed to support good people, to sustain a broad concept of relevance to disease, and to extend the freedom of the investigator. We now turn to some of these policies.

Basic Operating Policies and Objectives

There is, first, the operational policy of relying heavily on scientific advisers, grouped together as "study sections," to provide advice both on the capabilities of the person or persons and on the quality of the research proposal. The judgments and actions of the study sections are reviewed by other advisory groups, the National Advisory Councils, which consist of representatives of the public at large as well as scientists, and which make final recommendations to the Surgeon General. This reliance on rotating groups of technically qualified advisers is, essentially, a means of securing a sound consensus of peers. The advisory system provides a bulwark against arbitrary, uninformed judgment, and is, in this sense, a device for extending the effective freedom of all investigators as a group.

A second policy objective is extension of stability of support for investigators. Assured continuity of financial support is, in the final analysis, directed toward extension of the freedom of the investigator. It permits continuity of effort and thought of the investigator, undisturbed by an annual personal fund-raising drive. Over the past 5 years, it has been possible to extend from 20 to 50 percent the proportion of research grants that receive support for 3 to 5 years and to cut the proportion of 1-year grants from 50 percent to 10 percent. It is hoped to increase still further the proportion of grants made for these longer periods.

It is relevant to ask why a principle of operation which is obviously sound should not be applied even more rapidly and widely. The answer is that a balance must be sustained between support of new and younger investigators and those who are already receiving support. When grants of long duration consume a substantial part of any fund for research support, the amount available for new grants in any given year is relatively small even with an expanding budget. As in the case of many aspects of administration of research grants, the problem is not how to attain a single clearly defined objective but how to compromise between equally sound and sometimes mutually exclusive goals.

A third general objective for the research-grant program is to increase the average amount of the individual grants in order to provide funds in amounts sufficient to permit broader leeway to responsible investigators.

Over the period 1951–1955, the average (mean) new grant increased only from $10,300 to $10,800. The median grant in 1951 was $7600, and in 1955 it was $8400. When one considers that prices rose by about 10 percent over this period, the real value of the average new grant in 1955 was quite close to the real value of the average in 1951. On the other hand, it is worth noting that, in 1955, 37 new grants were awarded for annual amounts in excess of $30,000. The average amount of these grants was $47,000. One dollar in every six for new grants was for a grant in excess of $30,000 a year; and these grants totaled $1.7 million a year. Serious discussions with the study sections and the national councils that advise the National Institutes of Health have shown a unanimous desire on the part of members to see the broad research programs of additional numbers of thoroughly competent and prudent investigators supported through grants of substantial proportions for relatively longer periods of time, and to provide for investigations that may be described in terms of general rather than limited areas of interest. This is a major means of extending the freedom of mature investigators under a program of research grants, and there will be steady movement in this direction.

There are, incidentally, substantial advantages to the investigator in receiving funds in large segments from one or two sources rather than small segments from a large number of sources. The primary advantage is that differing sources of funds have different reporting require-

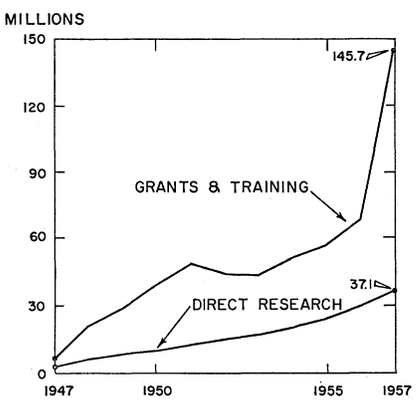

Fig 5. Annual appropriations to the National Institutes of Health, 1947–1957, by type of program.

ments, accounting requirements, and the like. The more numerous the sources of funds, the more time must be spent in writing reports and in performing nonproductive chores of various kinds. For this reason, it may well be that diversity of sources of support for medical research, which is widely accepted as a desirable national objective, should not be attained primarily through the support of single investigators by a large number of grants and contracts. The limits of such a course of action will be set by two factors—the total volume of funds available, and the desire of investigators to seek support from a single rather than a multiple source.

A fourth policy area relating to freedom of the investigator is the frequency and detail in which the investigator must report changes in the substance of his investigations, changes in the use of granted funds, and the progress of his work. Investigators who receive grants from the NIH file general reports at widely spaced intervals and report the substance of their work in the professional journals. Precise reporting to the NIH of scientific findings in the form of "progress reports" would serve little purpose, and publication in the journals seems preferable.

Investigators can and do, without asking permission, shift the emphasis of their studies in response to new leads that may develop.

Two procedural changes having to do with the handling of funds illustrate a general point with respect to the administration of research grants. First, investigators who receive grants for more than 1 year may carry over unexpended balances until the end of the recommended period of support. This replaces the earlier rule under which balances unexpended in any year would be returned to the Government. The new procedure produces additional flexibility and should result in more effective use of granted funds. The second change relates to freedom to shift grant funds among various kinds of expenditures—salaries, supplies, and so forth. Expenditures may now be made for the most part at the discretion of the grantee without checking with the NIH institutes. For example, if work evolves in a way requiring a major shift in expenditure to permit the employment of additional people, the change may be made without requesting permission. The reduction in paper work and the increase in flexibility is apparent. Some limitations, however, are placed on shifts in expenditures from the pattern stated in the grant application. Grantees may take foreign trips not provided for initially in the grant budget only after securing permission from the advisory body. Moreover, funds for direct research may not be shifted to indirect costs such as overhead.

These changes are important not only insofar as they are sound, but also because they illustrate the manner in which policy actually evolves. Rarely is a radical shift made from one way of doing business to another. Policy is the cumulative result of a series of related steps, no one of which may be particularly significant in itself. Rules are adjusted and modified with general objectives in mind —in this case, those which assure the greatest practical freedom for the investigator commensurate with the public interest.

Problem of Balance

One of the most intricate and elusive problems facing those who administer public and private plans for the support of medical research is how to attain and maintain an appropriate balance among three interdependent elements of a broadly conceived program: (i) current research support, (ii) training of manpower, and (iii) provision of adequate research facilities. The funds that are provided through the NIH are such a significant portion of the nation's total medical research effort that these interrelations must be a matter of concern. Reducing this abstract statement to the realities of the present scene, it appears quite clear that the attainment of sound balance among the three elements of research support call at this time for increased emphasis on training of manpower and on expansion of research facilities.

Here again it should be stressed that Congress is aware of the shortages of well-trained investigators and of laboratory space. The report that was submitted this year to the House of Representatives by the Appropriation Committee stated: "The Committee calls particular attention to the urgency of taking steps at this time to ensure that an adequate supply of medical research scientists will be available in the years ahead. No aspect of the Federal program for support of medical research is more significant than manpower training" (2).

As is true of research grants, funds for training will be markedly expanded in the year that began 1 July 1956. The appropriation for research fellowships and training grants totals $33.5 million, as compared with $17.3 million in the preceding year. This volume of funds will support a substantial expansion of training activities and at the same time will highlight certain fundamental problems of education. These relate to the size of the total annual pool of physicians and basically trained scientists from whom the nation's supply of medical investigators is drawn, to the complex set of difficulties involved in the quality of science teaching at all levels, and to deeply imbedded cultural values that are not most conducive to the maturing of scientific talent.

While NIH has no direct and formal responsibility for these broader aspects of science in American life, it does have

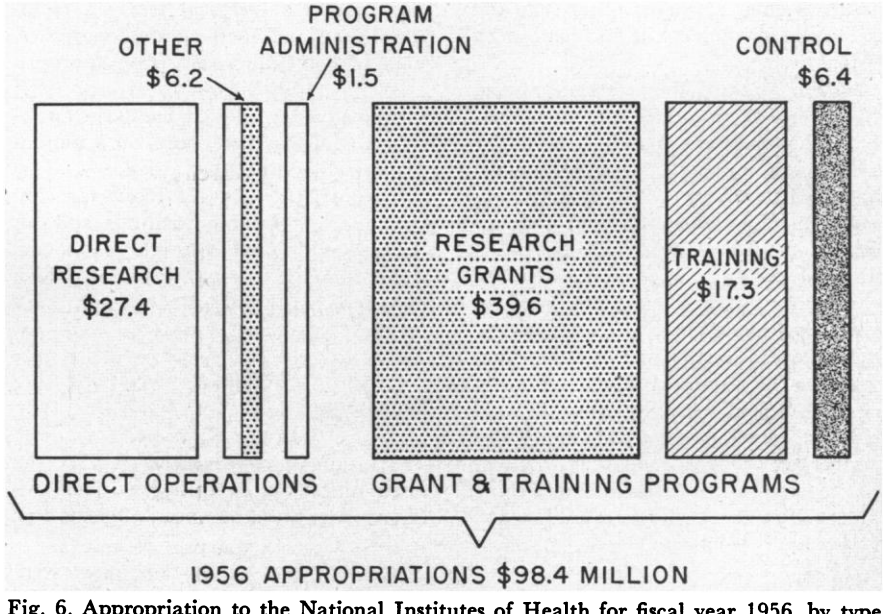

Fig. 6. Appropriation to the National Institutes of Health for fiscal year 1956, by type of program. The category *Other* includes the following: professional and technical assistance, $3.5 million; review and approval of grants, $1.3 million; biologics standards, $1.3 million; and dental resources, $0.1 million. The Control funds were transferred to the Bureau of State Services for grants to states.

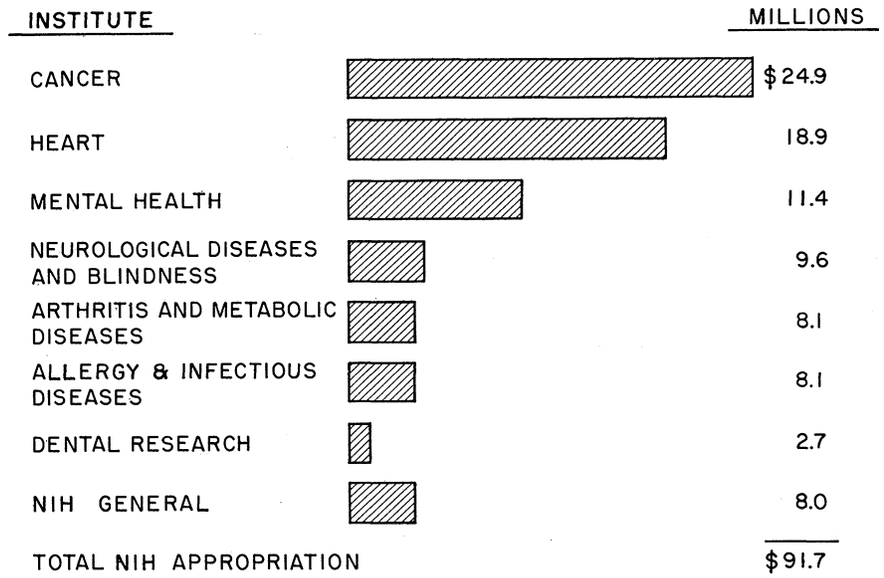

Fig. 7. Appropriations to the National Institutes of Health for the research-grant programs, fiscal year 1957, by categorical institute.

a clear obligation to sense emerging needs in the area of advanced training in biology and medicine and to adjust the nature of training programs to meet these needs. With extensive advice from the academic world, two specific problems have been identified as particularly significant.

1) There are well-recognized deficiencies in the training of physicians for careers in research. Rarely does a physician receive the rigorous training in research methodology that is typical of the Ph.D.-type of training. Experiments devised by medical schools and designed to remedy this weakness for students who intend to enter research rather than the practice of medicine will be financed by NIH.

2) The state of the sciences basic to clinical medicine—the preclinical sciences—has for some time been a matter of concern among those who have thought extensively about medical research, medical education, and their interrelations. These fields are becoming progressively more important as the essential unity of biological and medical sciences with the physical sciences is expressed operationally in the design and execution of experiments. Despite unparalleled need for a vigorous effort in this field, research is not flourishing. The number of younger men of top caliber who aspire to research and teaching careers in medical schools is inadequate.

As one means of improving this situation, NIH is offering senior research fellowships with sizable stipends for 5-year periods. These are awarded to relatively mature investigators as a means of attracting persons to and keeping them in the preclinical sciences. Senior research fellowships totaling $500,000 will be awarded this year, and the program will be expanded to a level of $2.5 million in $500,000 annual increments.

In connection with the need for more adequate laboratory space, legislation that authorizes the appropriation of $90 million to the Public Health Service over a 3-year period for assistance in the construction of medical research facilities was enacted by the 84th Congress. A total of $30 million has been appropriated under this bill for fiscal year 1957, a new advisory council has been established, and the first grants on a matching basis have been awarded.

Through provision of funds for construction of research facilities and for training additional research manpower, a situation has been averted in which expansion of grants alone could have created imbalance.

Conclusion

To return to the mission of NIH, the "extramural" program is now quite different from the program of 10 years ago. The word *project* has been defined and interpreted to provide greater flexibility; the volume of paper work has been significantly reduced. The duration of support has been increased, and there has been a broad geographic spread as more and more institutions have developed research interests and capabilities. The training program has been broadened in many ways to meet both general and quite specific needs.

The major point to be made here is not the substance of these changes but the fact that the research grant and training programs have changed, are changing, and will change in the future. Productive science is dynamic, just as a productive society and economy are dynamic. A federal program operating in such a complex, shifting environment must change if it is to serve most effectively. Responsible and responsive administrators of federal research programs have a very real and significant obligation to act so that federal activities increase the productivity of research and the vitality of training. There is a clear obligation to serve as the instrument through which these means are met through change.

It seems virtually predictable that the relationship between medical research and medical education will be an area of utmost importance and one in which significant changes will be made progressively over the years.

If the changes are to be wisely conceived and executed, administrators must act on the basis of sound, widely representative advice. Never in the history of medical science and medical education has it been so important that close, sympathetic understanding be sustained between private research groups, universities and medical schools, industrial research groups, and federal agencies. The extension of federal aid to medical research and related training over the past decade has created an unprecedented situation, one in which the actions taken federally are of such significance that wide participation in the decision-making process is essential.

References

1. Report on the Departments of Labor, and Health, Education, and Welfare, and Related Agencies Appropriation Bill, 1957, 84th Congress, 2nd Session, Senate Report No. 2093 (1 June 1956).
2. Departments of Labor, and Health, Education, and Welfare, and Related Agencies Appropriation Bill, 1952, House of Representatives Report No. 1845 (2 March 1956).