Medical Research and Medical Education[1]

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WHEN VANNEVAR BUSH'S IMAGINATIVE AND PRODUCTIVE REPORT to the President, *Science the Endless Frontier,* was issued in 1945, the major problems facing science in this country appeared to be expansion of support for research, particularly basic research, and the development of scientific talent in the youth of the country. Since then, the increase in funds available for research from both private and public agencies has been rapid. Money from both sources is now available for most fields on a scale that would have seemed visionary in 1945. With reference to federal funds for basic research and for fellowships in medicine, for example, Dr. Bush's report said, "After a program is under way perhaps 20 million dollars a year can be spent effectively." The U. S. Public Health Service alone supported medical research and fellowships in medical schools, universities, and other institutions at a level of about $18,000,000 in 1951.

Even though most areas of basic research could productively absorb larger funds, and although some fields of basic science are still meagerly supported, problems other than assurance of financial aid are becoming increasingly acute.

In the field of medical research, it appears to the Public Health Service that the major questions at this time relate, not so much to means of providing funds as to the development of policies ensuring that the objective for which federal funds are made available—promotion of basic research in medicine—is achieved most effectively. These policies must also ensure that the most productive relationship between medical research and medical education is established.

The Public Health Service is keenly aware that the research grants it is distributing to investigators in medical schools have a direct bearing upon the productivity of the nation's medical research program. Moreover, the grants have both direct and indirect effects upon the teaching function of the schools. Teaching is the major function of medical schools. For this reason, any activity of the Public Health Service—including provision of funds for research—affecting the performance of the teaching function must be most carefully considered to determine whether it affects teaching adversely or favorably.

Concern expressed by our advisers over the total effect of the grants for which we are responsible led us, in 1948, to request a group of outstanding men to assess just what these grants were accomplishing, and what problems they were creating. The group was known as the Surgeon General's Committee on Medical School Grants and Finances. Under the chairmanship of Lowell Reed,[2] vice president of The Johns Hopkins University, the committee produced a thorough report on the financial status of medical schools and on the relationship of federal research grants to the functioning of medical schools.[3] Most of the facts that we shall cite were unearthed by this committee, and many of the general considerations of policy subsequently discussed are the outgrowth of problems identified by the group.

One problem that merits the closest consideration is the effect on science of large-scale research in medicine and related fields—and the relationship of the federal government to the recent expansion of large-scale research. We are fully aware of a sharp cleavage of opinion in scientific circles on the degree to which research can or should be planned, set within a program, and be carried on by organized groups.

Dr. Conant, president of Harvard University, has succinctly phrased the essence of this debate: "The more uncommitted investigators the better . . .;" [however], "forces tend to increase the emphasis on programmatic research. . . . But if it be true, as I believe history shows, that the significant revolutions, the germinal ideas, have come from the uncommitted investigator, then the present trend holds grave dangers for the future of science in the United States."[4]

Dr. Bronk, president of The Johns Hopkins University, has said, "There is a grave danger that the present demand by publicists, industrialists, and public administrators for large-scale scientific organization may impede progress."[5]

Few thoughtful persons will deny that the dangers are real. The Public Health Service is, we repeat, directly and deeply involved in these matters, as are all private and public agencies now supplying funds for medical research.

Do our activities, by increasing the funds available for medical research, lead to excessive gadgeteering? Do they lead to a situation in which the nation has too few "uncommitted" investigators? Is it possible that the grants we administer create a threat to the freedom of science? We would like to present a point

[1] Based on an address by Dr. Scheele at ceremonies commemorating the one hundredth year of continuous medical education in Tennessee, University of Tennessee College of Medicine, Memphis, Oct. 4, 1951.

[2] The members of the committee were: George Baehr, Robin C. Buerki, Edward A. Doisy, R. G. Gustavson, Algo D. Henderson, E. E. Irons, Carlyle Jacobsen, Hugh J. Morgan, B. O. Raulston, James S. Simmons, and Herman B. Wells.

[3] *Medical School Grants and Finances, A Report by the Surgeon General's Committee on Medical School Grants and Finances.* Washington, D. C.: Public Health Service Publication No. 53, G.P.O. (1951).

[4] Conant, J. B. *Science and Common Sense.* New Haven: Yale Univ. Press, 320 (1951).

[5] Bronk, D. W. *Science,* **109**, 477 (1949).

of view on these questions based, first, upon our concept of the relationship of the Public Health Service to medical research in medical schools and universities and, second, upon our experience and study.

In our opinion, it is a mistake to assume that the pressure for large-scale medical research is the direct result of the large amounts of money now available. If there is undue emphasis in this country upon large-scale, programmed research, it is the result of intellectual forces that stem from society and from the scientific world itself.

This trend arises in part out of changes in the characteristics of research. The exploration of the underlying physical, chemical, and electrical characteristics of protoplasm and of biological systems is perhaps the most significant movement in medical research in this country. These investigations commonly require the combined talents of people trained in diverse disciplines. They usually require a degree of precision in observation and measurement that can be secured only by the use of complicated instruments. In addition, experience during World War II and since has shown that a concerted, planned attack on some problems produces valid results in a shorter period of time than could be expected from the uncoordinated efforts of individuals. All these forces have combined to enhance the magnitude of many investigations.

One cannot, however, remain blind to the possibility that data collection can supplant creative thinking, that some investigators may be intrigued by size itself. It is possible that the major syntheses of thought required for striking advances in science will occur less frequently if too many competent investigators are involved in coordinated research.

We are firmly convinced that the Public Health Service—or the federal government—should not attempt to set any general policy on this issue. Rather, we must allow the scientific community to decide, on the merits of each case, who and what should be supported, and the extent and nature of the coordination—if any—appropriate to each case. Any other stand by the Public Health Service would constitute a real and major invasion of the freedom of research.

We do believe that continuing expansion of medical research, including manpower and facilities for research, is in the national interest, and that the nature, approach, and organization of the expanded effort should be determined by a consensus of competent scientists. How far medical research should be expanded in relation to other fields is not a matter that we are competent to judge. The formulation of basic policy on the proper size of the nation's total research effort and on the proper division of emphasis by fields seems to us to be a long-range function of such bodies as the National Science Foundation.

What, then, is the role of the Public Health Service?

Its role is, in our view, to establish and maintain a mechanism which ensures that decisions truly reflect the collective judgments of those concerned with medical research and medical education. In this way, we intend to maximize the freedom of individual scientists to choose the extent to which they will be committed. This mechanism is a structure of eighteen technical panels, each composed of about twelve specialists selected from outstanding investigators in medical schools and universities. These panels are called "Study Sections." Their function is to review grant applications from prospective investigators.

The recommendations of Study Sections are reviewed by one of seven National Advisory Councils. The Study Sections have been set up administratively, but the councils are statutory bodies, and they include representatives of the general public, as well as scientific members. These groups not only review grant applications but also advise the Public Health Service on questions of general policy.

Errors in major scientific strategy—such as, for example, promoting a degree of large-scale research not in the best interest of scientific progress—can be committed by people of narrow vision, or by people who are unconsciously prejudiced by their own scientific or personal interests. This danger we seek to avoid through rotation of membership on our advisory bodies and by a most careful and discriminating selection of members. We believe that our councils and our Study Section groups are broadly representative, competent, and open-minded—so far as these virtues can be possessed by a group of human beings.

The origin of the research proposals considered by these advisory groups is of the utmost significance in any general assessment of the role of the Public Health Service. Subjects for investigation and the general scope and nature of the experimental approach are, with rare exceptions, set by individual scientists or by their institutions.

Although the Public Health Service only occasionally suggests areas for study, we believe that we have a positive responsibility to stimulate and even to plan investigations in particular circumstances. A Public Health Service investigator, for example, found that penicillin was extremely effective in the treatment of syphilis. We then stimulated a large-scale, controlled experiment involving a number of universities and medical schools. Clinical tests were designed to determine the most effective size and timing of dose. Within a short time, answers were produced that would have been available only over a period of years if the task had been left to the uncoordinated efforts of individual investigators. The same procedure was followed in the case of a coordinated study of the efficacy of streptomycin in the treatment of tuberculosis. To take another example, we have supported widespread studies of cortisone and other steroids. A similar large-scale coordinated research program on blood and plasma volume extenders is now in progress. These undertakings are typically financed by special Congressional appropriations, and not by contracting the scale of basic research support.

Coordinated studies are discussed with the appropriate National Advisory Councils, and one of the councils must, by law, recommend these grants, as is

true of all research grants, before they can be approved by the Surgeon General.

Whenever circumstances warrant, we shall undoubtedly launch large-scale research programs and persuade investigators to take part in them. As has been true in the past, however, they will remain a relatively small part of the total program. Studies such as these are largely applied research, and some of them do commit investigators to a definite research procedure. In our judgment, however, they are clearly in the national interest, and the medical research potential of the nation should be adequate to encompass them, as well as fundamental research by uncommitted investigators.

Most of our research grants have been made within the framework of Congressional appropriations for broad disease categories, such as cancer, heart, and mental health. Under such a system, it is conceivable that only applied investigations specifically and demonstrably related to specific diseases would be supported by the Public Health Service. However, we and our advisers are convinced that, if this philosophy were to prevail, the basic phenomena which will explain these diseases would elude discovery. For this reason we encourage the widest range of basic investigation. There is virtually no aspect of fundamental medical research that is not being supported by Public Health Service research grants, and such studies comprise the bulk of the work supported.

In this connection, we have urged that studies relating to narrowly defined diseases or disease groups not be set apart for support through institutes with narrow missions, but rather that they be grouped so that undue emphasis upon applied research can be avoided. Congress has accepted the principle that medical research cannot be best advanced by setting up small research compartments.

The form in which our research grants are made, as well as the total volume of grants and the general fields that they cover, affects investigators. Our grants are for research projects—for investigations outlined in advance by the experimenter. There are, of course, certain risks in such a system.

First, inadequate attention to the capability of the investigator—as contrasted with the outline of work that he proposes to undertake—can lead to serious errors. Our advisers do give the qualifications of the applicant, whether he is a recent graduate or a seasoned investigator, heaviest weight in arriving at decisions. In our opinion this is the only sound policy to follow.

A second potential danger inherent in any project grant system is that the grant may be administered so that the investigator may feel restricted in formulating and following his project. We do not require that investigators follow in detail the work outlined in their project applications. In practice, we believe that those whose work we help support do in fact have adequate elbow room to follow leads and hunches.

A third aspect of the project system is the tendency to remove elements of scientific decisions from the medical school and university, and to reduce the flexibility of the institution's research program. This is without doubt one result of any project system of awarding grants, whether the source of the funds is governmental or private.

A fourth criticism of the project system is that it does not provide adequate continuity of support. Uncertainty seems to be characteristic of life, but our effort is to ensure the maximum continuity of support attainable under annual Congressional appropriations, and consistent with other important but conflicting objectives of a grant program. We feel, for example, an obligation to remain constantly aware of the fact that overemphasis upon continuity can preclude support of some new ideas and of some younger and promising investigators. At present, about 40 per cent of the Public Health Service research grant funds are going to investigators whose work has been continuously supported for three to six years. Whether that percentage should be increased, decreased, or left unchanged is a question that we and our advisers keep constantly in mind.

The Public Health Service, since the inception of its large-scale research grant activities in 1946, has considered solving these four problems by shifting from project grants for individual investigators to a system of block grants for institutions, for departments in institutions, or for broad research programs. There is a great deal to be said for a system that permits medical schools and universities to use the money to support a total research program framed and planned on a long-range basis by the institution itself.

This is a matter, however, on which sharp division of opinion is encountered. Many investigators and some deans of medical schools feel that recommendations as to support of individual investigators made by Public Health Service Study Sections, and similar public and private groups, are sounder than those that might be made within their individual institutions. Many administrative officials prefer to have decisions on research support made outside their own institutions. The formulation of criteria that will provide a guide to the most equitable and productive distribution of block grants to institutions presents a set of thorny and unresolved problems. As a public agency we would hesitate, for example, to establish a system under which we would have to select a few institutions for block grants. On the other hand, if block grants were made to all medical schools, universities, and research institutes, the grant to each would be quite small.

In view of the divergence of opinion, we have asked a group composed of representatives of each of the advisory councils to study the question and to make recommendations to us. At the same time, the Public Health Service staff is gathering an extensive body of fact and opinion, analyzing the information, and reviewing the basic elements of policy that have to be considered in arriving at a decision. This procedure is time-consuming, but we feel that questions

of this nature can be soundly resolved only through broad participation of people with varying viewpoints.

The impact of our research grants on research is no more important than their effect upon the teaching function in medical schools. The dependence of a fully productive teaching program upon adequate links to research is axiomatic. In years past, the establishment of modest research opportunities for faculty members was a major problem. Now the concern is reversed. Many deans worry about ways and means of sustaining a modest amount of teaching of reasonable quality in the presence of a large and growing research structure.

Two basic facts reveal the source of this concern. Since 1941 the basic operating expenditures of medical schools have just about doubled. These are the funds from which salaries are paid, from which equipment and supplies are purchased, and through which buildings and equipment are maintained. They do not include capital expenditures. When account is taken of the sharp price increases over the past ten years, the actual purchasing power of the general operating funds has expanded quite modestly.

On the other hand, research funds have increased more than fourfold since 1941. Even when 1951 dollars are considered in terms of 1941 purchasing power, the scale of research in medical schools has expanded tremendously since the beginning of World War II. The relatively large increase in research funds from both private and governmental sources can be attributed to the postwar upsurge of interest in all research by the general public, and particularly to the drama and appeal of medical investigations. The financial plight of medical schools and the relationship between protection of health and the adequacy of support of the schools have recently had an encouraging result; nevertheless, the failure of the less glamorous teaching function to attract adequate support has created some very real problems, which may be briefly reviewed.

When a medical school accepts a research grant, it incurs costs additional to the direct costs of the research project itself. The school must supply utilities to the laboratory where the project is carried on. It must provide library service to those engaged in the project. It must maintain grounds and buildings. The Public Health Service allows an additional sum—8 per cent—of each project grant for these indirect costs. With rare exceptions, this is not enough. We have not, however, seen our way clear to expand indirect payments at the expense of payment of direct costs; and without larger appropriations from Congress additional payments for indirect costs would result in the denial of grants to investigators in some institutions. We feel that some universities and medical schools are prompted to request the Public Health Service to bear the full direct and indirect costs of research not because they consider this a sound relationship, but because they are now operating under extreme financial pressure.

Large research grants have a direct effect upon the staffing of medical schools and upon salary structures. It should be noted that the Public Health Service makes grants to support not only research, but teaching related to cancer, mental health, and heart disease. These teaching grants have proved extremely valuable but, all things considered, these advantages are obtained at a substantial cost, because some schools have had to employ additional faculty members to carry the teaching load as research has expanded. Moreover, the grants have exerted indirect upward pressure on the general salary structure. In the words of the committee that reviewed the effect of the grants, "The problem is that the schools are hard put to finance these desirable changes, which are in effect forced upon them by the grants."

In the long run a sound teaching structure in medical schools, in our opinion, can be established only by a marked increase in general operating funds and not by proliferation of teaching programs directed toward specific diseases.

A third major effect of increased support of research has been to stimulate the development of new administrative arrangements for the conduct of research. Some of these involve the creation of research institutes or similar organizations that do not follow the traditional pattern of attachment to either the medical school or university science departments. Others involve less formal grouping of research organizations around individuals. In many respects these new patterns seem to be an adaptation to the changing nature and needs of medical research and are productive. Such adjustments suggest that the full volume of medical research performed in universities and medical schools cannot always be accommodated as an enterprise that is directly linked to the teaching function, or otherwise fully integrated with the medical school structure.

One cannot foresee what patterns of organization for medical research will evolve, nor what kinds of relationships may develop between medical research and medical education. There are, however, unmistakable signs that the process of transition is painful. For example, some investigators attached to semiautonomous medical research organizations have no university tenure, and hence lack the degree of security conducive to long-range research productivity. Tenure for these investigators would require financial commitments that many schools cannot undertake because the general financial resources of medical schools are inadequate.

In short, we attribute much of the stress and strain that appears to arise out of the administration of the Public Health Service grant programs to a deficiency in financial resources. In itself, the expansion of medical research has been a clear gain to the nation. Hence we believe that the problems created by uneven growth of research as compared with general support should be resolved by expansion of resources and not by curtailment of research.

The relationship of research to higher education is

not, of course, a problem peculiar to medical research. The vast expenditures on basic and applied research and on development by the armed forces and the Atomic Energy Commission are critically important to the nation's defense. The effect of this accelerated program will permeate the entire structure of higher education. Universities and colleges will be feeling the same financial pinch that medical schools have lived with for some time. It seems quite likely, therefore, that the balance between research and teaching will be a matter of increasing concern. A continuing reappraisal of the net effect of expanded research upon the teaching function, and of the steps required to sustain the quality of both, is urgently needed. We, as well as other agencies, need the guidance of the National Science Foundation and other qualified organizations.

We have explored only a few of the questions of policy that confront us. We have not, for example, been able to explain the Public Health Service research fellowships. In our view, expansion of the pool of highly trained research manpower is as important as the support of work in progress. We believe that the 1,400 fellows whom we have aided to date will, within a few years, contribute significantly to the furtherance of medical research and teaching.

By discussing some specific questions we have tried to indicate what we believe our role to be and how we propose to carry that role out. Underlying all the specific problems is a sense of living and working in an era of transition to patterns that cannot now be foreseen, but which will be different from those of the prewar years. As this evolutionary process moves forward, we are deeply conscious of our responsibilities as public servants. We must keep open the channels of communication between educational institutions and the Public Health Service, and we must formulate our policies on the basis of the most sensitive and intelligent appraisal of trends in medical research and education of which we are capable.

Although we have dealt primarily with unresolved problems, they should not obscure the far more important fact that medical research is advancing rapidly. We believe, indeed, that the medical research of the country is now as alive, intellectually vigorous, and productive as in any period of our history.

Technical Papers

The Effect of Temperature on the Molluscacidal Activity of Copper Sulfate

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In recommending copper sulfate as a molluscacide, Chandler (*1*) states:

> There are a number of factors which influence the effect of copper sulfate on organisms in water, the most important being temperature, presence of algae, alkalinity, and organic matter in solution. As regards temperature, no extended experiments were carried out, but experiments with a 1 to 1,000,000 solution were carried out at temperatures of from 15 to 27° C, and the snails apparently succumbed as quickly at the lower as at the higher temperature.

The contradictory nature of these two statements regarding the effect of temperature has never been satisfactorily resolved. It is the purpose of the present study to show that the first of Chandler's statements rather than the second is correct insofar as the effect of temperature on the molluscacidal activity of copper sulfate is concerned.

Observations by other workers as to the bearing of temperature on the activity of molluscacides have been infrequent and inconclusive (*2, 3*). More recent work by Kuntz and Wells (*4*) and by the present authors has led to the conclusion that temperature is a factor of primary importance in determining the activity of molluscacides.

In the present series of experiments the response of *Biomphalaria boissyi*[2] was observed at five temperatures in the range 14°–26° C, using concentrations of copper sulfate pentahydrate varying from 0.05 to 100 ppm. The selected temperature range approximates the seasonal variation in water temperatures in Egypt (*5*).

Snails for these tests were collected from an irrigation drain near Cairo. The collections and tests were carried out between Feb. 24 and May 18, 1951. Four hundred selected snails measuring from 9–14 mm in diameter and weighing 200–350 mg were kept for 48 hr in a battery of four 15-liter aquaria, which, in turn, were surrounded by a water bath maintained at 25 ± 0.5°. Oxygenated tap water was circulated through each aquarium at the rate of approximately 100 ml/min; an excess of a local variety of spinach (*sabaneh*) was also supplied. Continuous illumination was furnished by two 15-w daylight lamps suspended 10 in. above the aquaria. Snails that had undergone this conditioning treatment appeared to give a more nearly uniform response than those used immediately after collection.

Samples of water from local canals and drains har-

[1] The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

[2] The intermediate host of Egyptian *Schistosoma mansoni*.