Basic Science in Mission-Oriented Endeavor

Shannon on pragmatism; Weinberg and Orlans disagree on the role of the university in basic research.

Recognizing that research and development cannot continue to grow indefinitely at an exponential rate, scientists have become increasingly concerned about the prospects for ample support of basic research and especially about the public tendency to confuse the relatively small "seed" expenditure for this activity with large expenditures for developmental or applied purposes in the space and military fields.

In response to the growing concern about the role of basic research in the total R & D picture, Fred Snell (State University of New York at Buffalo) organized a panel discussion on "Basic science in mission-oriented endeavor" for the recent Biophysical Society meeting in Houston.

Panel members, chosen to represent a mission-oriented agency, one of the largest mission-oriented laboratories, and a critical sector now confronting the physical and biological sciences from other parts of the academic world, were: James Shannon (director, National Institutes of Health); Alvin Weinberg (director, Oak Ridge National Laboratory); and Harold Orlans (Brookings Institution). Philip Abelson (editor of *Science*) was chairman of the panel.

Orlans, an anthropologist and sociologist who has drawn blood in important places by suggesting that some kinds of science may have already advanced more than enough, said he was there "to represent the ignorant public, the taxpayers, and perhaps even a body which some say is both ignorant and taxing: the Congress—one of the most important strongholds of unbridled and unpredictable individualism still surviving in this nation of massive monopolies and conformities."

After this winning introduction, Orlans, who has just completed a staff inquiry on federally financed social research for the Reuss Subcommittee on Research and Technical Programs, settled down to point out that: ► While the *rate* of growth has been checked, basic research is still growing, and the annual increase in public expenditure for basic research is larger than increases for applied research and development. ► As the money goes up, the character of research changes—"I fear that it will be on average of lower quality." ► The time of the doctrine "that you can never do too much basic research" has passed.

While NIH has "hit upon a genuine union of a practical and a pure purpose" and is a "practically successful model, at the moment and in the present temper of Congress," Orlans said that the academic community would rather have the money come through the National Science Foundation.

"Mission-oriented is a terrible expression, and I wonder if it really means anything else than 'all *other* agencies but the National Science Foundation!'" Orlans also suggested that "government expenditures for basic research" should simply be translated as "government expenditures for academic research." If this support were to come through the National Science Foundation, the academicians would "not only get the money but they would feel that they are somehow being rewarded for themselves, that the virtue of pure science is acknowledged and recognized by the Congress." Orlans added that he thought it vain to hope for such funding through NSF.

Spectacles from Mount Palomar?

Orlans gave little indication that he himself was awed by the "virtue of pure science," at least in the physical sciences. For example:

"If basic research can often (not always) be good for practical people (manufacturers, engineers, politicians), I want to suggest that applied research can also (not always) be good for impractical people (physicists, professors, and impolitic men). I see no convincing reason why a modest amount would not be desirable at the National Science Foundation (as Congressman Daddario has proposed), at Kitt Peak (dare I also suggest, at the Carnegie Institution—wouldn't Mount Palomar be an excellent place to develop a new binocular or spectacles?) or, indeed, in the innermost sanctum of modern scientific purity, the prestigious university."

Weinberg disagreed. "I believe the unversity, on the average, is *not* the proper place in which to launch integrated, massive attacks on mission-oriented problems."

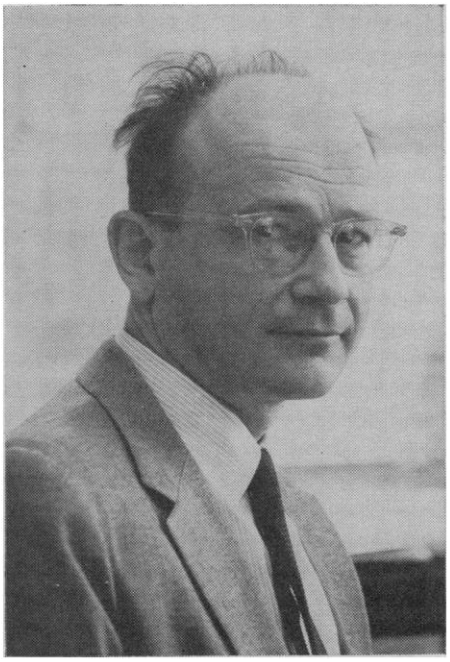
Nor did Weinberg agree that the National Science Foundation should support applied research. "In my own experience the most fruitless kind of applied science is applied science done in abstracto."

"Large interdisciplinary research establishments which are mission-oriented, make no excuses and are not self-conscious about their dedication to a practical mission, yet maintain a strong flavor of basic science, strike me as the proper instruments for getting on with much of our applied business. In medical research one might point to Roswell Park or Sloan-Kettering; in communication, to Bell Laboratories; in electrical industry, to General Electric or Phillips to illustrate the strength of these institutions.

"I would suggest that where missions have been clearly defined, and where the general path toward accomplishment of the mission is reasonably clear, each government agency ought to use the multidisciplinary, multicontract institute as its proper instrument rather than broadcasting hundreds of very small contracts throughout the land.

"Of course where the path is not clear—where what is being sought is a point of departure—where one can make *no* predictions as to where a breakthrough will appear—then the multicontract method is obviously the proper course. . . .

"Where feasibility has been established, the role of basic research is primarily to set standards, and to help with incremental discoveries; where feasibility has *not* been established, the role of basic research is to hit upon the breakthrough—hopefully by a sin-



Orlans: has some science advanced enough?

gle lucky discovery (as the discovery of fission) but more usually by a gradual increase in understanding that finally yields a coherent picture (as seems to be happening in the field of protein synthesis).

Biomedical Research in Prefeasibility Stage

"To my mind, most of biomedical science is in the prefeasibility stage—everyone would like to cure cancer, but no one knows how. In this field, broadly speaking, what is needed is widely supported basic research, since the necessary breakthrough cannot be ordered in advance and is the more likely to come the more different groups are involved. Some of this exploration should take place in the multidisciplinary institution, but a great deal, perhaps more, should be done in individual, and imaginatively led, small laboratories."

Weinberg also said that the interdisciplinarity and the intimate relation between basic and applied research in large mission-oriented laboratories, both industrial and government, have been responsible for the great success of many applied scientific missions in the postwar years. He referred to the proposal, made by a number of scientists, that large mission-oriented laboratories, "rather like the Atomic Energy Commission National Laboratories," be set up to study problems in the life sciences—for example, environmental factors in disease.

One reason basic research is vital as a part of such a mission-oriented laboratory, Weinberg said, is that applied research has less of the "ruthless interaction and self-criticism" characteristic of basic research with its tradition of open publication in refereed journals. Basic scientists in a mission-oriented laboratory transfer their standards of excellence both to colleagues working in applied programs and to management.

How to Answer the $1 Billion Question

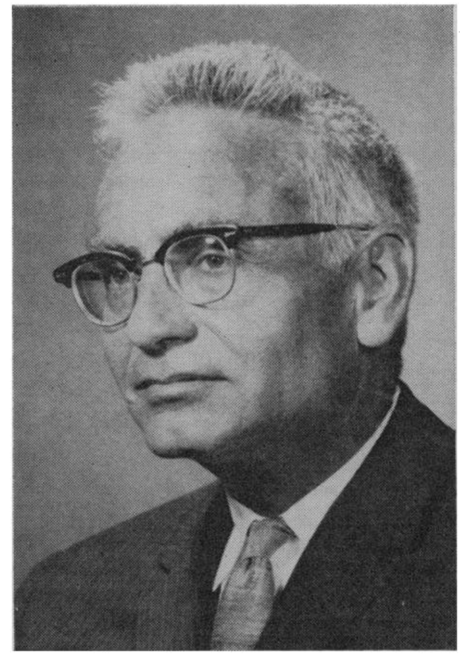
The present store of fundamental knowledge in the biomedical sciences does not permit "a direct onslaught on disease problems," Shannon said. "I consider the resources of NIH to be effectively deployed only if they contain a mix of fundamental, applied, and developmental research. Without broad fundamental inquiry, the ultimate solution of our problems will not be possible."

When Shannon became director of NIH in 1955, the total budget of this mission-oriented agency was $98 million. This year its funds amount to $1.1 billion—an increase of ten times. No dispenser of the public purse has ever matched Shannon for success: he has won nothing less than the complete confidence of the scientific community and, more unexpectedly, the Congress.

For those who have wondered, with some envy, just how Shannon has brought it off, his remarks at the symposium gave some clues. He made it clear that a wise administrator is a pragmatist, free from the illusion that there are "absolute answers" and able to temper his objectives to the winds of change.

"I think all you can do is examine the present situation for research. If it is inadequate, how should it be improved? If it is too lush, where would be the best place to cut it back? The level of expenditure for either basic or applied research will always depend in part on the health of the economy as a whole and will always compete with the other tasks our economy must do.

"I don't really differentiate in my own mind in a very precise way between what is basic and what is applied research. . . . I am much more concerned in seeing certain work done and giving certain work a strong push regardless of the purpose of the scientist who happens to be doing the work. His purpose may be to cure cancer but his work may be in the field of fundamental virology."



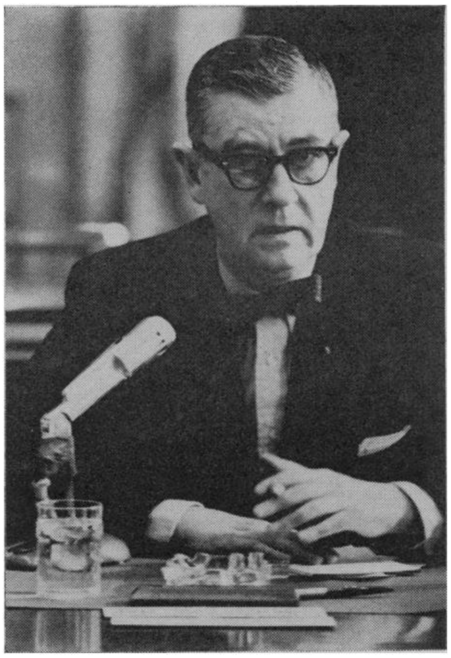
Weinberg: small lab can lead in basic studies

Shannon indicated that the pragmatic administrator must sense when it is time to deploy support into certain scientific fields. "For a period of 20 years or so, microbiology didn't have much to offer and didn't warrant much more than minor support. As frequently happens, developments in collateral areas of science and collateral areas of technology suddenly permitted this field to take over. It is now moving very, very rapidly and contributing very broadly to our understanding of many phenomena. As a pragmatist, I would say that this is an area that even at the expense of other areas we would support as broadly as possible.

Push toward Biophysics

"After much discussion, we reached in 1955–56 a judgment that there was much in the physical sciences that could be applied very broadly in the biological sciences. We did a fairly extensive search to find out how many persons with first-rate training in physical sciences were indeed involved in the biological sciences. How many departments of physics were recognizing that biological material might be of some interest to their graduate students?

"We found that very few depart-



Shannon: how biophysical research increased [Joan Sydlow]

ments of physics had any interest in biology and that there were very few researchers in biophysics. Judging the potential contribution of physics to biology to be large, we set up a study section, with F. O. Schmitt as chairman. With Council approval, a revolving fund of $100,000 a year was granted. They toured the country and put on five seminars in depth that involved the major departments of biology and departments of physics in each of the five areas of the country. The study section was empowered to commit any part of the $100,000 to fellowships, either short-term or long-term grants, training or whatnot, with the agreement that we would blanket this support into our normal program.

"The result was that some extraordinarily effective physically oriented people became broadly preoccupied with some substantial problems in biology. I think it is reasonable to estimate that excellence in biophysical research had increased by a factor of 10 or 15 times within 5 years after we initiated this activity. . . .

"I think the interaction between fundamental and applied research as we see it in our own laboratories is extraordinarily intimate and extraordinarily productive. . . . I think the broad underpinning of basic research has become increasingly important in all fields. I suspect we will not again go through another period of invention like that of Edison's day, when rapid progress was made without understanding of the basic phenomena. . . .

"The educational process would be quite sterile without day-by-day fundamental inquiry." Shannon estimated that a minimum science base in support of medical education would require the equivalent of about two full-time researchers in each preclinical department and the equivalent of about four full-time researchers in the larger, clinically oriented departments. A science base at this level would cost about $2 million a year. He said that about one-third of the medical schools in the U.S. are below this dollar standard and the adequacy of their science base is open to question. It has been estimated that 25 additional medical schools will be built or initiated before 1975. Thus perhaps $100 million annually is needed to provide a more adequate science base for the educational process itself.

Shannon also pointed to the lack of cancer research over the country as a whole (main centers are in Buffalo, New York, Bethesda, and Houston) and to a similar lack of distributed research in the cardiovascular field.

Whatever their differences on specifics, the panel seemed in agreement that scientists will not have the last word on how much support will continue to be given to basic research in a "society that is itself mission-oriented," to use Weinberg's apt phrase. This decision is surrounded by political questions that reflect the most basic values of a society. Few scientists share, for example, the majority opinion supporting heavy commitment of our resources to land a man on the moon, an amount of dollars large enough, Lord Bowden estimated, to feed and clothe half the undeveloped world.

When Weinberg said, "We have decided that sending a man to the moon is worth $5 billion and that achieving better health for our society is worth $1 billion. I think that happens to be a wrong allocation between these two objectives . . ." he was interrupted by sustained applause. All those who attend scientific meetings know how unusual this sort of response is.

"Of all applied scientific activities," Weinberg added, "none strikes me as being anywhere near so important as answering the age-old questions related to the elementary human suffering of premature death and unnecessary disease."

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Cell, Tissue, and Organ Culture

The relationship between the cultured cell or tissue and its in vivo progenitor was investigated at a 2nd Decennial Review Conference, held in Bedford Spring, Pennsylvania (10–14 September 1966). It was felt that a need existed to define the role of tissue culture as a tool or as a discrete entity worthy of investigation in its own right.

Three impressions concerning the ontogeny of cells in vitro emanated from the Conference. One impression is the extreme lability of most of the cells in an original explant, the plasticity of a minority of the cells, and the question of the homogeneity of such a cell population. Although Patricia Farnes (Rhode Island Hospital) pointed out that the established cells derived from explants of bone marrow seem to be a perivascular fibroblast by histochemical tests, it is not obvious whether the fibroblasts are a homogeneous cell population or whether the enzymatic marker reflects only coincidental identity. It is this overriding problem of adaptability and the limits thereof that would cause one to have reservations about Stanley Gartler's (University of Washington School of Medicine) rather sensational statement that all cell lines examined by him to date are contaminants of the HeLa strain. Could not the genetic variant of glucose-6-phosphate dehydrogenase, peculiar to the Negro, which he found in HeLa and in the other 18 lines tested, be a reflection of either a selective process or an induced change? Intimately associated with the matter of cell plasticity is the influence of environment. Here it was interesting to see how the work of Harold Ames (Harvard Medical School) and Katherine K. Sanford (National Cancer Institute) complemented each other. The former spoke of uncharacterized activator molecules in serum which in his hands served as positive signals to maintain the differentiated biochemical phenotype. Sanford, addressing herself to the question of spontaneous malignant transformations, remarked that cells of most animal species frequently alter in vitro; this alteration can be reproduced within definite time intervals by such factors as different sera in which carcinogenic agents cannot as yet be identified.

Quite obvious to all was the debt that biology owes to the in vitro system. Without this system much of what is now accepted as facts of tissue and cell interaction would still be unknown.