Book Reviews

The NIH Phenomenon

Politics, Science, and Dread Disease. A Short History of United States Medical Research Policy. STEPHEN P. STRICKLAND. Harvard University Press, Cambridge, Mass., 1972. xvi, 330 pp. $9.95. A Commonwealth Fund Book.

This book is the definitive history of a phenomenon unique in the history of science—the rise to political power of biomedical research. After World War II, what had been the National Institute of Health, a small-time microbiological laboratory, was transformed into the National Institutes of Health, a vast machine for the support of a nationwide biomedical research effort. Stephen Strickland has meticulously put together an absolutely first-rate historical account of the political aspects of this metamorphosis, with all of the pressure, tension, and personality affinities and conflicts involved. He has done this with a remarkable sensitivity to all the forces that were at work and with an evenhanded, skeptical, humorous, and penetrating understanding of a most remarkable cast of characters and series of events. I say these things with a high degree of confidence because over most of the years covered by the book it was my privilege to be the chief of the Office of Research Planning at the National Institutes of Health. Only those who were firsthand participants in the movement can appreciate the comic irony of that title. Planning research from that vantage point at that time was like controlling a meat grinder from the inside. Anyhow, it did provide day-to-day contact with many of the significant events chronicled in the book, and an opportunity to help shape some of them.

The central thesis of the book (to reduce a rich story to a threadbare outline) is that a set of strong forces combined after the war to produce a research program of great scope, scientific force, and effectiveness. These forces were—believe me, not in order of significance—Congressman John Fogarty and Senator Lister Hill as strong proponents in Congress; a strong lobby led by Mary Lasker; a brigade of extraordinarily persuasive scientists and physicians who understood the importance of convincing Congress of the power of biomedical research; a group of nonprofessional professional lobbyists who served the cause more for love than money; and James A. Shannon as the leader of NIH and the political spokesman for the academic community. One of the most amusing threads that runs through Strickland's account of affairs aptly traces the manner in which each of the major figures in the drama claims the central role.

Finding some critical remarks to make about the book has been difficult. The author might have given more emphasis to the ripeness of the scientific conditions in the years following the war. He does take the importance of "readiness" into account in dealing with the cancer chemotherapy program, but he does not generalize the point, which is an important one. The NIH expansion would have been a gigantic boondoggle if the biosciences had not been at the point where further scientific advances were possible over very broad fronts. Indeed, it is dangerous to use the NIH experience as a precedent for analogous efforts in other areas unless scientific readiness is carefully assessed.

In fact, scientific readiness was not assessed in the early days of NIH. It was simply fortunate that when the political steamroller went into action the field was ready, and, moreover, a large group of scientists left scientifically underemployed by the conclusion of the war could turn their minds and hands to biomedical research. Thus, the rapidly rising investment caused increases in scientific output rather than simply the inflation that would have been the consequence of pouring money into the work of a fixed number of investigators. One can in fact, as the current phrase goes, attack problems by throwing money at them, but it will go down a well if the basic preconditions for effectiveness are not present. In this connection, one thinks of the history of community mental health programs, regional medical programs, and recent experiments with elementary and secondary education.

The generally cavalier way in which NIH, safe from coercion or retaliation by reason of its allies outside the Administration, treated its nominal hierarchical superiors in the Department of Health, Education, and Welfare and the White House raises interesting questions related to the operation of the federal government. A thoughtful friend once scolded me gently after I had described to a university seminar the way NIH operated in defiance of the executive branch, the President, and the Bureau of the Budget. He said, "What would happen if all agencies operated that way?" The answer is, of course, that government would be in a complete shambles, rather than in its chronic state of substantial disarray. I felt a twinge of conscience at the time at being a party to such a subversion of orderly government. But since then, three conclusions have eased my mind: (i) government is likely to sit on its dead center if there are not occasional revolts in the hills, (ii) one need not worry too much that the grouping of forces required to produce the NIH phenomenon will come about often enough to subvert the government, and (iii) it is a relief to have a life-oriented powerhouse at work now and then to demonstrate that the general welfare is as important as the common defense. So if anybody or any group can put together a coalition that will do as much for the common cause, or for any special worthy cause, as the NIH coalition did, applause is in order—even at the risk of irritating the political satrapy.

One important aspect of the NIH story is missing from the book, that is, the ambassadorial role it played as the link between the world of politics and the world of science. On the one hand, NIH was head over heels in the political game that Strickland describes sensitively and accurately. The purpose of this frenetic activity was to get money. On the other hand, the people at NIH bore a heavy responsibility for nurturing a scientific enterprise of great significance. The record of NIH in using federal funds to foster science deserves the highest marks on all essential counts. Look at the record:

1) Maintenance of a high degree of freedom for investigators and institutions while federal funds for them grew in absolute and relative terms.

2) Sensitive awareness and judicious

fostering of new scientific fields, such as physical chemistry and molecular biology.

3) Establishment of the first institutional support grants.

4) Maintenance of an adequate balance between the legitimate needs of institutions and those of individual investigators.

5) Fostering of wide direct participation of scientists in the decision-making process. (This point alone is most significant in a general political sense. The peer review, "study section" device of assessing requests for support is a powerful means not only of securing broad participation but of ensuring the decentralization of decisions, improving communication within the system, and monitoring all aspects of its operation.)

6) Deliberate efforts to diversify the medical science structure of the nation.

7) Fostering basic medical sciences while operating a system based essentially upon a disease approach.

8) Developing broad, integrated approaches to investigation through the establishment of research centers, while enlarging the scope of the system based essentially on the project grant to the individual investigator.

9) Deliberate expansion of the manpower base for biomedical research, through expansion of fellowships and training grants.

10) Avoidance of political interference with the operation of the system of support of science.

It was no minor accomplishment to guide such a scientific effort on the one hand while simultaneously engaging in the complementary political game on which Strickland concentrates. The pressures were often diametrically opposed. Speed, expansion, action, flashy public appeal, and the glamor of public figures characterized the lobbying effort, as was appropriate. The NIH contingent, led by Shannon, attempted to moderate or redirect the force of the more politically oriented lobbyists with a view to making the total effort more productive. This was an equally appropriate effort, but this objective view of the situation conveys no sense of the ferocity of the will of the two parties to prevail. The NIH staff, on whom fell almost the whole responsibility for designing the strategic elements of the scientific effort, had to act simultaneously as scientific statemen, administrators, and political figures. Who did what in this complex arena would make an interesting book in itself. In fact, the two areas of effort—working out the policies essential to a sound scientific effort and getting the money to support the research—were not entirely separate. Take one example from among many that might be chosen. Congressional support for a large element of basic science was clearly essential if the total undertaking was to be productive. Yet most congressmen and senators were interested in the cure of disease and not at all concerned with the essential underpinning of basic work. I say "most" because Fogarty, Hill, and some others understood the role of basic research fully, and supported it. Their attitude, as Fogarty said to me one time, was, "We'll get the money. You fellows spend it." This was not *entirely* the case because, as Strickland points out, Fogarty and others in Congress did press for specific, focused support for research on disease entities. But these areas of support were a minor part of the entire budget; the NIH apparatus had and still has a remarkably free hand in deciding what to spend money on, and the conditions surrounding the expenditure of funds.

Lest I be misunderstood, it must be added that the institutes and the NIH director's office did not interfere at all with the "retail" decisions on who would get what grant. What the central apparatus at NIH did was to influence the "wholesale" distribution of funds by broad area. It left the specific "retail" decisions to study sections. This is a mode of operation that can reconcile the conflicting requirements that science be responsive to the general public will and that professional judgments determine the quality of the investigators.

How was congressional assent to the use of categorical disease funds for basic research to be secured? First, the record of the appropriations committees in both the House and the Senate was packed with testimony by persuasive and articulate scientists on the need for basic research. This helped. More important, a deal was struck with John Fogarty. Over the years a congenial accommodation was reached on the preparation of the reports of the House and Senate committees on appropriations—a document having the force of law and one which in the absence of authorization hearings actually substituted for substantive legislation. The deal was that Fogarty would insist on backing research on a series of specific diseases that had not been the subject of intensive research. (Here he and the lobbyists were right and the NIH view was generally too conservative.) In return, he gave NIH a free hand to write language supporting basic research, and within limits, setting the support levels for basic research. The NIH staff actually wrote the reports of the House and Senate appropriations committees for a number of years. In this capacity, the NIH staff scolded itself for lack of vision, urged itself on to new heights, made miscellaneous pronouncements on the state of science, and plugged for support of research on neglected diseases. Interestingly enough, the necessary lobbying with the members of the House and Senate, apart from Fogarty and Hill, was done by the extraordinarily effective lobbyists drawn together by Mary Lasker and the disease-oriented associations. The NIH role in Congress was confined almost entirely to working with Hill and Fogarty.

These observations on the times gone by are offered not to criticize Strickland's book for omissions but to indicate the kinds of thoughts that a good book can provoke. Anyone who has a serious interest in the relationships between government and science ought to read the book, not only to absorb history but to think upon the changing scene and the relevance of the NIH story to the present and the future.

The book concludes with an account of the enactment of the Cancer Act of 1971. But what an extraordinary conglomeration of people and pressures it took to stave off by narrow margins a series of strongly supported and potentially disastrous proposals. Senator Edward Kennedy and his staff, with an eye to political aggrandizement as much as to cancer research, proposed that a new National Cancer Authority be established under the direction of an administrator appointed by the President and confirmed by the Senate. A new Cancer Advisory Board would be established with an equal number of lay and professional members. Adoption of this proposal would have separated cancer research from the mainstream of biomedical research, and would have weakened NIH and thereby weakened the most effective structure for support of biomedical research that the world has ever known. This bill passed the Senate by a vote of 79 to 1, after Ann Landers, confidential adviser to some 50 million readers, at the request of Mary Lasker stimulated an avalanche of mail in its behalf. Then the Senate

action was upset in the House by a campaign that brought into action a new coalition. Paul Rogers, Chairman of the Subcommittee on Public Health and Environment of the House Committee on Interstate and Foreign Commerce, emerged as a thoughtful, solid, and effective congressional leader. The Association of American Medical Colleges exerted new strength as a spokesman for the academic community. Equally important, the scientific community was aroused and vocal. The new array of forces was basically different from the alignment during the '60's. Then John Fogarty's appropriation subcommittee both controlled appropriations and in effect wrote substantive law. In 1971, the legislative committee took control of the substantive decisions. The scientific and academic community took on the Lasker forces and won. The position of the White House was somewhat different during the two periods. Earlier the Administration simply opposed increases in appropriations for medical research on the scale proposed by Congress, and was routinely overridden. During the debate over the Cancer Authority, the White House wobbled so severely in a search for immediate political advantage that it had only minor influence on the ultimate outcome.

So the saga continues to unfold. The "heart people" will certainly seek parity with cancer research, and the other major disease entities will not be far behind. At this point, it looks as if the cancer episode will initiate a new cycle of increasing federal appropriations for biomedical research after the doldrums of the last few years.

Finally, and this is a point which Strickland does not stress, biomedical research is now debated in the context of the full range of problems related to the maintenance of health—delivery systems, the economics of health, the development of an adequate cadre of health manpower, and so forth. From 1945 to about 1970, biomedical research was the major national health program. Over that period, the nation was in no mood to consider seriously the nature of the public responsibility for the health of the population, and how this responsibility might be exercised. Hence research was the happy beneficiary of a national aspiration which could during those times be expressed only indirectly and partially. This accounted in large part for the outpouring of funds through the federal government. Support of research was the only respectable way in which legislators could simultaneously respond to the desire of people to do something about disease and their aversion to anything smacking of—to use a quaint phrase—socialized medicine. Other avenues are now opening before them.

Note added in proof. The recent dismissal of the director of NIH, Robert Q. Marston, was an event foreshadowed by the extension of NIH activities into areas of direct concern to the President. However, Marston was dismissed apparently not because of policy differences but simply because he was appointed during the Johnson Administration. Some way must be found to recognize both that the director of NIH does indeed have broad policy responsibilities and that back-of-the-hand treatment of this post as if it were a routine administrative job can cause irreparable harm to an important national institution. The answer must be to establish by law new selection procedures and criteria for the position, roughly analogous to those governing selection of the director of the National Science Foundation. The entire problem should be thoroughly reviewed in congressional hearings. This is something the scientific community could help to bring about.

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Fluoroacetate, Etc.

Carbon-Fluorine Compounds. Chemistry, Biochemistry and Biological Activities. A Ciba Foundation Symposium, London, Sept. 1971. North-Holland, Amsterdam, and Elsevier, New York, 1972. viii, 418 pp., illus. $18.75.

For many chemists, biochemists, toxicologists, and pharmacologists mention of carbon-fluorine compounds may call to mind a pesticide and rodenticide called "1080," known more scientifically as sodium fluoroacetate. Some may recall that this compound proved to be the active principle in a poisonous South African plant, and some may even remember it as exemplifying Sir Rudolph Peters's concept of "lethal synthesis," since it must be converted in vivo to fluorocitrate to become biologically active. For many years the status of C-F compounds could be succinctly described by two principles: if they can be metabolized to fluoroacetate, they will be highly toxic; and since F can readily masquerade as H and the C-F bond is apparently very stable in vitro, some fluoro compounds might enter into certain biological processes in such a way as to deceive one or another enzyme.

More recently Peters and P. W. Kent came to the conclusion that the time was ripe for an interdisciplinary meeting to consider the status of knowledge of C-F compounds. This volume records that meeting. That the situation has indeed progressed beyond the early concepts built around fluoroacetate is clearly brought out by the exciting papers presented here. It is readily apparent how much greater is the research potential and challenge of these compounds than was originally thought. The subject matter included is chemical, biochemical, and biological in nature, and though each paper basically fits one of these categories, each contains much that is appropriate to the others. This is equally true of the discussion following each paper, and of the three separate sections devoted to general discussion.

The expansion of knowledge is reflected in a more diverse use of fluoro compounds as metabolic probes, in investigations of microbial pathways of metabolism and enzyme systems, and in the development of therapeutically useful fluorine-containing drugs. Each of these subjects is discussed in this volume, and each in more than one paper. For example, as metabolic probes fluoro amino acids are now used to study amino acid uptake and amino acid and protein synthesis and fluorosugars are used to study membrane transport of sugars. These compounds, and fluorine-containing macromolecules, have been of use in studying the mechanisms of action of a variety of enzymes. Studies of microbial metabolism often are of wider applicability, and fluoro compounds have proven useful here; several instances of the rupture of the C-F bond by microbial enzymes are now known. Fluorinated pyrimidines and fluoro steroids are now among the most biologically potent analogs known of the naturally occurring compounds.

As a biochemically trained toxicologist, this reviewer must give pride of place to those papers that deal with the mechanism of action of fluoroacetate, still incompletely understood. The principal features of the toxicity and be-