Philip Handler: An Appreciation (13 August 1917–29 December 1981)

DeWitt Stetten, Jr.

Philip Handler's many achievements in world affairs should not mask the fact that he was fundamentally a scholar. We can detect early evidences of this scholarship in his weekly visits to the community library as a small child. According to his mother, he would withdraw seven volumes, the maximum allowable, returning those which he had consumed during the preceding week. This habit of reading abundantly and omnivorously persisted throughout his life. It certainly contributed to his early intellectual development, leading to a baccalaureate degree at the College of the City of New York before his 19th birthday and a Ph.D. in biochemistry 3 years later from the University of Illinois under the preceptorship of Herbert E. Carter.

Handler then joined the recently established faculty of Duke University School of Medicine where he remained until he was called to assume the presidency of the National Academy of Sciences in 1969. He climbed the academic ladder at Duke achieving the Chairmanship of the Department of Biochemistry in 1950 and was named James B. Duke Professor of Biochemistry in 1961, a title which he still had at the time of his death. He was surely one of the leaders of the Duke faculty which earned for that school its high position as a source of well-trained physicians and of gifted investigators in the biomedical sciences. He sponsored many graduate students and authored many important papers, particularly in relation to the metabolism of nicotinamide, biological oxidations, and the biochemical aspects of Darwinian evolution.

During these years Handler served on many important advisory groups. He was elected president of his major professional society, the American Society of Biological Chemists, in 1962. He was a member of the National Science Board and served as its chairman from 1966 to 1970. He also participated in many advisory functions at the National Institutes of Health during the period of the Institutes' most rapid growth. He was a firm advocate of the concept of training grants and an early proponent of the notion that in addition to the categorical institutes there ought to be at least one institute dedicated not to a disease area or an organ system, but rather to the support of the basic medical sciences. This notion ultimately led to the establishment of the National Institute of General Medical Sciences.

In addition to his more than 200 papers in scientific journals, Philip Handler was a coauthor with the late Abraham White and with Emil Smith and myself of *Principles of Biochemistry*, first published in 1954. He persevered as a contributor through the first six editions and was anticipating continued participation in the seventh edition at the time of his death. His remarkable familiarity with current developments in the field of biochemistry in the face of many demands upon his time and effort was certainly in part due to his continuing association with this work. His great breadth of knowledge, his familiarity with the litera-

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ture both past and present, and his keen insight into biological processes made him a particularly valued coauthor.

Philip Handler was essentially a private person and was slow to reveal his emotions. His immediate family, composed of his wife Lucy and their two sons, Mark and Eric, was a closely knit unit. My own children benefited from their inclusion in the extended Handler family.

The 12 years during which Handler served as president of the National Academy of Sciences were marked by many important events. Two of these deserve special mention. Under his leadership the Academy assumed a positive position in the support of scientists in other lands whose civil liberties were being abrogated. It became a function of the Academy to explore such cases as were brought to its attention and to rise to the defense of scientists in other countries whose rights were being abused. In this as in most other regards Handler was a staunch liberal, a political stance in which he was strongly supported by his wife.

Philip Handler

A second memorable event related to the creation of a monument honoring the 100th birthday of Albert Einstein. Washington is, of course, a city of monuments but curiously, despite the great impact which science has had on our way of life, only one statue, that of Joseph Henry, commemorates the accomplishments of a professional scientist. Therefore, to honor Albert Einstein, the services of a sculptor were retained and a monument was designed to be placed on the lawn in front of the National Academy of Sciences building on Constitution Avenue. Despite a wave of criticism in the public media attacking both the concept and the design of the monument, Handler persevered and, as he foresaw, it has become one of the attractions of downtown Washington. Approximately 3 years ago the memorial was dedicated, and Handler was able to derive particular satisfaction from watching the many children who climb on the statue to be photographed next to Albert Einstein by their parents.

At about the time of the meetings of the National Academy in April 1980, Handler's friends became aware that something was amiss. Soon thereafter he was diagnosed as having a lymphoma. He was, however, determined to complete the term of his office, devoting all possible attention to his job. Although his health was visibly deteriorating he did remain in the position of president of the National Academy of Sciences until 30 June 1981, thus completing his second 6-year term of office. He then withdrew to Woods Hole, Massachusetts, where the Handlers owned a home with a particularly beautiful view of the setting sun which they all enjoyed. About 1 month later he was hospitalized in Boston and it was there that he died of pneumonia on 29 December 1981.

During his life, Philip accumulated a large array of prizes and medals in addition to 29 honorary degrees. He also delivered countless lectures at many institutions. He was a man of few hobbies. It is true that of recent years he shared a sailboat with his successor, Frank Press, but this proved to be more an occasional relaxation than an engrossing hobby. He possessed a fine baritone voice and enjoyed singing with friends around the piano in his living room. His major avocation was clearly his chosen vocation, and conversation in his home rarely drifted far from the field of science. He had an unusually wide acquaintance among scientists, and with a select group of these he was an intimate friend. Those of us who were fortunate enough to be members of this inner circle rejoiced in its warmth and were stimulated by its conversation.

Philip Handler: His Research

Handler's interests as a research scientist were broad and encompassed diverse systems, from the whole animal to highly purified enzymes; he had valid credentials in nutrition and physiology as well as in biochemistry.

His earliest independent studies, mostly in collaboration with W. J. Dann and W. A. Perlzweig, concerned metabolic transformations of nicotinic acid, particularly as they applied to the vitamin-deficiency disease pellagra. His studies of pyridine nucleotide biosynthesis, performed with J. Preiss, are basic in the field of nucleotide metabolism, and illustrate the roles of adenosine triphosphate and glutamine in these processes. His studies of protein and amino acid metabolism, performed first with myself and then with G. Duda, provided a scale of metabolic activity for the various amino acids, and showed clearly the central role of glutamine. Amino acid transport studies in gut and kidney showed the competitive nature of amino acid transport. Other nutritional-metabolic fields to which Handler contributed were those of effects of salt and protein on hypertension, the role of parathyroid hormone in kidney function, and the role of labile methyl groups in metabolism.

Handler had broad interests in enzymology. His studies of phosphoglucomutase, with J. Joshi, were among the earliest to show structural and functional homologies in the active center of an enzyme in diverse species. His studies of the metalloflavoproteins xanthine oxidase and aldehyde oxidase, in collaboration with K. V. Rajagopalan and I. Fridovich, gave important information on the mode of action of oxidative enzymes with multiple redox groups. Studies of sulfite oxidase which, like xanthine oxidase, is a molybdenum-containing enzyme, were precursors to Rajagopalan's later studies on the structure of the pteridine-containing molybdenum cofactor.

The studies of the mechanism of xanthine oxidase and enzymatic and nonenzymatic sulfite oxidation revealed an important role of oxygen-containing free radicals; these studies led to Fridovich's discovery of superoxide dismutase.—HENRY KAMIN, *Professor of Biochemistry, Duke University Medical Center, Durham, North Carolina 27710*