NATIONAL ACADEMY OF SCIENCES

PHILIP HANDLER

1917—1981

A Biographical Memoir by

EMIL L. SMITH AND ROBERT L. HILL

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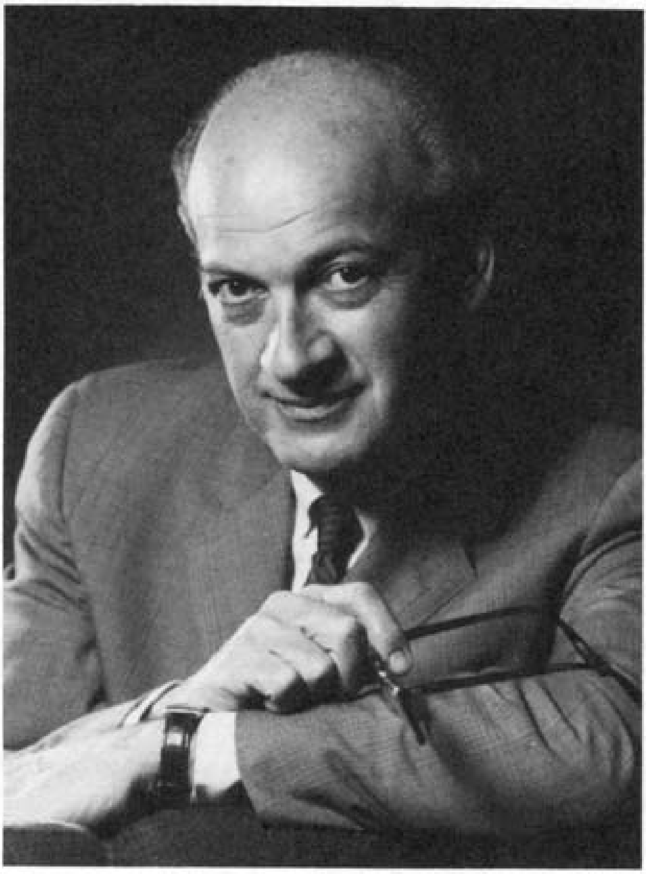

Photograph by Antony Di Gesu, New York, N.Y.

PHILIP HANDLER

August 13, 1917–December 29, 1981

BY EMIL L. SMITH AND ROBERT L. HILL

PHILIP HANDLER was the eighteenth president of the National Academy of Sciences and served two consecutive six-year terms from 1969 to 1981. His tenure was marked by a rapid growth of the Academy and by a great expansion and reorganization of the work of the National Research Council. It was also a period of controversy and political turbulence in the nation, and the role of the Academy in public affairs increased considerably. The work and character of the Academy will likely long be influenced by the many changes that occurred in these years.

Philip Handler was born in New York City on August 13, 1917, the first child and oldest son of Lena Heisen Handler and Jacob Handler. His mother, one of ten children, was the daughter of a chicken farmer in Norma, a town in southern New Jersey. The life of his father, who came from central Europe, represented an almost typical American success story of that immigrant generation, and served as an example to his family of the rewards that come from hard work, self-education, and determination.

Jacob Handler arrived in this country in 1903 at the age of fifteen, learned English in night school while working as a grocer's errand boy in New York City, then worked on a Pennsylvania Railroad road gang out of Altoona, Pennsylvania, for some years. He then got a job as mechanic-machinist at a roundhouse in Jersey City, New Jersey, becoming foreman in 1914. After he married Lena Heisen, whom he met while walking in New Jersey on vacation, he and his family moved to Brooklyn, New York, where he used his savings to buy a small gasoline station. His savings were wiped out in the difficult depression years of the early 1930s, but by his retirement in 1960 he operated an extensive chain of service stations on Long Island.

Philip Handler was brought up with two younger siblings, his brother Melvin and sister Rhona, in a home that was child-centered to a considerable degree. The family at first lived in modest circumstances, but later enjoyed a more comfortable situation. Summers until his thirteenth year were spent on the farm of his maternal grandparents, where Phil helped with the chores of feeding chickens, milking cows, and tending the vegetable patch. He had a multitude of cousins to play with, and as he recalled these early years, "family life in the summer revolved about a summer kitchen and was warm, mellow, gemütlich." It was also on this farm where his curiosity was first aroused about the nature of living things.

Partly out of need, partly out of wisdom, Phil's parents expected him to work at an early age. Thus, it became natural for him to spend summers working in gasoline stations through his high school and college years. Here he encountered the mechanical-electrical world and, although dissatisfied with the level of understanding of the typical mechanic-electrician, he also recognized that the competent craftsman was the "salt of the earth" and the backbone of our society. He recalled that his exposure to the diversity of people he met during these years taught him to judge a man by his merits, not his background.

Phil's parents also believed that formal education, which they lacked (his mother had attended a one-room school through the tenth grade), was the pathway to success and happiness. It was expected that he should study and make good grades. Study came easily, and his library card was over-used, one of the first indications of his love of books and his voracious appetite for knowledge. He was precocious in school and skipped many grades to graduate from New Utrecht High School in Brooklyn in his fifteenth year. Although he was the youngest member of his high school graduating class, he finished near the top and was elected president of the scholastic honor society.

Phil later noted,

> A few high school teachers stand out. One who taught biology was extremely rigorous and managed to convey both a sense of scientific discipline and a sense of wonder. The second, a woman who taught chemistry, infuriated me because she would not tolerate tangential questions or those which did not bear directly on her lesson plan. Withal, when I left high school it was with the feeling that, somehow, science was for me, although the branch of science was unclear. I suspect that a voracious appetite for science fiction was more significant in this regard than was high school itself.

The economic depression of the early 1930s precluded the notion of attending college away from home, and Phil entered the College of the City of New York in February 1933. He was graduated in June 1936, before his nineteenth birthday. Like many youngsters who advanced rapidly through high school and college, Phil found these years somewhat frustrating at times insofar as he could not compete in athletics with his contemporaries, who were three to four years older, nor could he participate fully in their social life. "Perhaps, in the long run, the latter was a boon since I was thrown back on my own resources and those of the library."

During his first college year, Phil thought about a career in medicine and majored in biology and chemistry. Indeed, in his junior year, he applied to and was accepted in several medical schools. Two things happened in his senior year of college, however, that diverted him from a career in medicine. As he recalled,

> First, I was aroused by the course in physical chemistry—and then angered. Why, I asked, had I been studying chemistry for three years only to be told the rules of the game as a senior. Second, I had a course in biochemistry with Professor Benjamin Harrow. It was he who finally lit the fire. An exciting, vibrant lecturer, he made it plain that although biochemistry was but a rudimentary science (1935–36), which had scarcely learned what questions to ask if life was to be understood, it must be in the language of chemistry. And I was converted.

After his retirement Harrow said that he remembered Phil as "one of the best half-dozen students I ever had," no small praise from a professor who taught biochemistry at City College for over thirty years and inspired many of his students to become biochemists.

Thus came a change of plans. Instead of entering medical school, Phil went as a graduate student, at Harrow's suggestion, to the University of Illinois to study with William C. Rose in the Department of Chemistry. There he studied in one of the great chemistry departments of the time with a galaxy of faculty stars, including Roger Adams, C. S. Marvel, R. L. Shriner, R. C. Fuson, W. H. Rodebush, G. L. Clark, B. S. Hopkins, and L. F. Audrieth, as well as Rose, who had just discovered the nutritionally essential amino acid, threonine. He decided not to work with Rose, however, but chose to do his thesis research with Herbert E. Carter, a newly appointed member of the faculty at Illinois; he became Carter's first Ph.D. student and lifelong friend.

Inasmuch as a scholarship was not available, Phil took a half-time post in the U.S. Department of Agriculture on the Illinois campus, in a nearby laboratory for study of soybeans and industrial byproducts. As a result, he worked concurrently both on his thesis research with Carter and at the soybean laboratory. Studies at the latter on the reaction between formaldehyde and proteins resulted in his first publications, which, according to Carter, could have made a satisfactory thesis by itself. Despite these dual activities, Phil received his doctorate in three years in biochemistry, with equal minors in organic chemistry and embryology.

We should like to quote some remarks that Carter made about Phil as a graduate student (cited by Thomas H. Jukes in a biographical sketch, *Journal of Nutrition*, 113, 1085–94, 1983):

> Phil's tremendous energy and ability to get things done rapidly and effectively were abundantly apparent even then. . . . He read voraciously—from chemistry to biology and philosophy. He . . . loved to discuss problems of all kinds—with wit and the fluency which so characterized his life. . . . He was a terrific story-teller with a knack for producing the appropriate tale to enliven a discussion or reduce a tension. . . . I have never met nor worked with a person who had Phil's selfless interest in aiding and stimulating others, and that terrific ability to understand and contribute to the activity and success of his colleagues has certainly been a trademark of his—which was clearly evident in my research group in 1936–1939.

Because of his interest in nutritional research, developed under the influence of Carter and Rose at Illinois, Phil chose to do postdoctoral work in Durham, North Carolina, at Duke University School of Medicine with William J. Dann, a Cambridge-trained nutritionist interested in human pellagra and a related disease in dogs, blacktongue. Thus began in June of 1939 Phil's forty-two-year association with Duke University, the only institution in which he was to hold a full-time academic appointment. He later recalled his first years in the "callow, nouveau riche atmosphere" of Duke University, "Dann was ill with severe, essential hypertension and while I benefited from his counsel, particularly his iconoclasm in scientific matters, I was, thenceforth, a free agent and independent investigator. More important to my education was the presence of Frederick Bernheim, a mature experienced student of intermediary metabolism at the level of tissue slices, homogenates, etc., from whom I learned much, both of lore and of technique."

Nineteen thirty-nine was an equally important year in Phil's life; after he had been at Duke only a few weeks, he married Lucille Marcus, whom he had met at the University of Illinois while she was an undergraduate student. Lucy and Phil Handler were devoted to one another and celebrated their forty-second wedding aniversary the year he died. Throughout their lives together, Lucy was continually supportive of Phil's career. With their two sons, Mark and Eric, they formed a close-knit family, with many friends in the scientific community, not only in Durham and later Washington, D.C., but also in Woods Hole, where they spent many summers.

The postdoctoral wanderings that Phil had planned for himself were prevented by World War II. As part of the war effort, the medical curriculum at Duke was accelerated to train more physicians, and the few faculty available to teach medical students were overburdened. Thus he was to spend the war years as an assistant professor of physiology, pharmacology, biochemistry, and nutrition and taught all of these subjects to medical students in their basic science years. At the end of the war, he transferred entirely to the Biochemistry Department, where he was to teach and do research for the next twenty-four years.

RESEARCH CONTRIBUTIONS

Philip Handler had a broad range of research interests throughout his career. After beginning research in the general area of biochemical aspects of nutritional deficiency states, he was to extend his activities to coenzyme metabolism, renal hypertension, the mechanisms of hormone action, amino acid metabolism, biological oxidations, the mechanism of action of enzymes, and biochemical evolution. The following account of his research accomplishments does not include many of his studies in these diverse areas but only those that the authors, in retrospect, believe greatly influenced his career or provided his most significant and lasting contributions.

Phil's first efforts in biochemical research at Illinois gave him a body of theory and technique on which he would build his future research career. In addition, he wrote many years later that he also learned the important lesson of how to collaborate with others. His thesis research with Herbert Carter also taught him a valuable lesson that he recalled later,

> With Dr. Carter I performed two major studies, the nutritional capabilities of N-alkylated and N-acylated amino acids, respectively. This required development of novel synthetic procedures and these were followed by nutritional experiments. All proved successful and the data stand, although their interpretation remains difficult. It is of interest that, among these, were the synthesis and feeding of α- and ε-acetyl lysines as well as α,ε-diacetyl lysine. The data were in conflict with notions then widely held and hence, were not published. Yet precisely the same studies were performed as the doctoral dissertation of Fred Sanger, at Cambridge, some eight years later, with precisely the same results. Their publication taught me that experimental observation, judiciously and honestly conducted, is the first obligation of the experimental scientist and that theory must be compatible with observation, not the reverse.

Phil's first important scientific publications dealt with the biochemical aspects of pellagra, a disease then prevalent in the southern United States that results from a dietary deficiency of a vitamin, nicotinic acid. He and his colleagues, primarily W. J. Dann and William A. Perlzweig, with special methods they developed, determined the nicotinic acid levels and pyridine nucleotides in the tissues of normal and vitamin-deficient animals. These studies established a link between the disease and the metabolism of the vitamin.

An interesting observation Phil made at this time was that the signs of blacktongue, the disease observed in nicotinic-acid deficient dogs, disappeared if sufficient infusions of saline were given. Subsequently, he noted that blacktongue was not a disease resulting from a lack of dietary nicotinic acid but rather a product of eating corn. Subsequently, others showed that corn was deficient in tryptophan, a dietary essential amino acid, which could serve as a metabolic precursor of nicotinic acid.

These studies, published in nine papers with Dann between 1940 and 1942, were the first of many that combined nutritional analysis and the intermediary metabolism of dietary substances. Thus, with Mary L. C. Bernheim and J. Raymond Klein he showed that sarcosine (N-methylglycine) was oxidized by liver homogenates to glycine and formaldehyde, one of the first demonstrations of the production of one-carbon fragments in metabolism. In addition, he developed the technique of feeding large quantities of nicotinamide to rats as a means of depleting all substances capable of donating methyl groups. Methionine was the only substance that when fed to methyl-group depleted rats was capable of alleviating the fatty livers and reversing the retarded growth of these animals. These studies established that one ultimate source of preformed methyl groups is methionine. Although methionine and choline had been shown by others to interchange methyl groups under normal conditions, stresses on the methyl transfer system revealed that methionine was the indispensible source.

During this period, Phil recognized that patients at Duke Hospital were treated for hypertension with a diet low in protein and salt. Stimulated by this observation and his previous studies on low protein diets in pellagra, he initiated studies on the effect of dietary protein levels in animals with experimental hypertension. It was found, with Frederick Bernheim, that very low protein diets relieved hypertension in rats but could be restored by adrenocorticotrophic hormone. Subsequently they demonstrated that animals on low protein diets fail to synthesize many pituitary hormones, each of which acts to enhance the demand for dietary protein. Turning off synthesis of these hormones protects animals with low protein intake.

Phil's interest in endocrine function led to studies with David V. Cohen on the purification and mechanism of action of parathyroid hormone. The preparations obtained were not homogeneous, but they were sufficiently pure to show clearly that a major mode of action of parathyroid hormone is to inhibit renal tubular reabsorption of inorganic phosphate, in accord with earlier proposals.

His investigations of pellagra also prompted Phil to study the biosynthesis and degradation of nicotinic acid. Accordingly, he showed that nicotinic acid administration to human beings gave rise to elevated levels of nicotinamide adenine dinucleotide (NAD) in erythrocytes. But the metabolic steps leading from nicotinic acid to NAD could not be elucidated until better analytical techniques became available. Thus, with Jack Preiss in the mid-1950s, three consecutive steps leading to NAD synthesis from nicotinic acid and ATP were elucidated. Moreover, the degradation of NAD was subsequently shown to yield nicotinamide and adenosine diphosphoribose. Based on these studies, Phil helped enunciate what has become a major biochemical principle: that major metabolic pathways are essentially irreversible in the organism, and the apparent overall interconversion of two metabolites usually proceeds by different metabolic pathways, each of which utilizes entirely different enzymes and intermediates.

Phil's interest in amino acid metabolism, which began early in his career, prompted the studies in the early 1950s with Henry Kamin that showed that the transport of amino acids across the intestinal and renal membranes is a competitive process. They also examined the ability of various amino acids to produce urea and concluded that glutamine plays a central role in the metabolic conversion of the amino acids and ammonia to urea. Later, with George Duda, he confirmed the central role of glutamine in mammalian nitrogen metabolism by showing that virtually all the nitrogen influx through the organism eventually passes through this substance. Subsequently, with Jack Klingman, renal glutaminase was isolated and characterized, elucidating other important aspects of glutamine metabolism. They also demonstrated that the amount of renal glutaminase increases in acidosis, one of the first demonstrations of an adaptive enzyme in a mammal.

In view of Phil's interest in nicotinic acid and the coenzymes it forms, it was quite logical for him to become interested in oxidative enzymes that utilize other vitamin cofactors. Accordingly, from the early 1950s until he gave up his research program, he and his colleagues examined the structure-function relationships of the mammalian metalloproteins, xanthine oxidase, aldehyde oxidase, sulfite oxidase, and dihydroorotic acid dehydrogenase. Largely in collaboration with Irwin Fridovich and K. V. Rajagopalan, the electron transport pathways from substrate through the several complex cofactors of these enzymes, and ultimately to oxygen, were elucidated. Particularly significant was the discovery, with Rajagopalan, that these enzymes contain iron sulfur centers, previously known only in proteins of bacterial oxidation-reduction systems. In addition, they were the first to show that sulfite oxidase contains molybdenum, an essential element for normal enzyme action.

Of special importance was the work with Fridovich on xanthine oxidase, in which it was demonstrated that for every hypoxanthine molecule oxidized to xanthine by the pure enzyme, hundreds or thousands of sulfite molecules could be oxidized to sulfate in a reaction dependent on molecular oxygen. This was shown in due course to be the result of a chain reaction initiated by the free radical, superoxide ion, which is formed when xanthine oxidase is reduced by its substrate and then reoxidized by molecular oxygen. This proved to be the first evidence suggesting that superoxide ions could be formed *in vivo* as a normal product of oxidative enzyme action.

In retrospect, the studies with Rajagopalan and Fridovich on oxidative enzymes were probably Phil's most important scientific contributions. Indeed, each of his collaborators in this work has continued independently to pursue the lines of research begun with Phil. Fridovich recognized that the superoxide radicals (and other radicals derived therefrom), produced by xanthine oxidase and several other systems that he discovered subsequently, could be very toxic to living things, and as some of the most powerful oxidizing agents known, these radicals could react with and destroy most biological compounds, including DNA, RNA, and proteins. Thus he was to discover the superoxide dismutases, the enzymes that protect all aerobic organisms, whether bacteria, plant, or animal, from the toxic effects of superoxide radicals. For the decade after their discovery in 1968, the superoxide dismutases were the most studied of all enzymes.

Rajagopalan was to continue examination of the structure-function relationships of the flavo-molybdoenzymes; from them, he isolated and characterized a previously unrecognized vitamin-like cofactor containing molybdenum, which he called molybdopterin. Later he helped demonstrate that rare but highly lethal mutations in the genes that control the structure of sulfite oxidase or molybdopterin synthesis occur in the human population.

One of Phil's last research interests was biological evolution. He demonstrated, primarily with Jayant Joshi, that the phosphoglucomutase from such diverse organisms as halobacteria and man were structurally similar. This observation, along with those of others concerning different proteins, helped strengthen the view long held by some, but not established well biochemically, that all living forms are derived from a common ancestor.

After his Ph.D. studies and postdoctoral training with Dann, Phil did not actually perform many of the experiments himself. This was partly because most of his collaborators were Ph.D. students or postdoctoral fellows who joined his laboratory to learn how to do research so that they might become independent investigators themselves. This required giving his young colleagues free rein to learn new techniques as well as to design, execute, and interpret their own experiments. (We should add that Phil developed a severe allergy to the white albino rat, and had rather dramatic allergic reactions when too near the animal room.) Nevertheless, Phil was intensely involved in his own research program, as well as those of others in the department. His door was always open to colleagues who wanted to discuss their research. Indeed, he got the greatest pleasure from even the smallest research progress of others, and he was never happier than when discussing the options for further thought or study that the experiments at hand suggested. He found it pure joy to learn something new, especially from scientific observations. One of us (R. L. H.), after joining the biochemistry faculty at Duke in 1961, was initially amazed at, but eventually grew accustomed to, Phil's ability, after being told of a new development outside of his research area, to recall it lucidly and clearly weeks and months later, and to incorporate it in the body of knowledge he used daily. Indeed, his quickness at grasping the details of a new body of knowledge, interpreting this knowledge in the broader context of the field, and then rapidly recognizing the best way to proceed productively, was not only a great strength in his research, but also an invaluable talent in his life as an academic, a public servant, and a science advisor to federal agencies.

ACADEMIC CAREER

Phil's talents became quickly evident within a few years after he arrived at Duke University. In 1945 he was promoted to associate professor of biochemistry and on the death in 1950 of William A. Perlzweig, chairman of the Department of Biochemistry since the founding of the School of Medicine, he became professor and chairman of biochemistry. At the age of thirty-two, he was probably the youngest biochemistry department chairman in an American medical school. He was made James B. Duke Professor in 1961.

Phil was to remain as chairman of the Biochemistry Department until 1969, when he resigned the post and took a leave without pay to become president of the National Academy of Sciences. University regulations at the time did not permit a professor at Duke more than two years leave of absence without loss of position. But on the recommendation of the Medical School faculty and administration, the Board of Trustees approved his reappointment with leave of absence every two years until his death. At that time, only one other Duke professor was so honored. His devotion to his University was equal to that of his University to him. Indeed, during his last year as president of the Academy, he visited the campus on several occasions to discuss his return to academic life and to consider how best he could use his talents and experience for the greatest benefit to colleagues and students alike.

One of Phil's outstanding abilities was his excellence as a lecturer in the classroom. He gave a large portion of the general biochemistry course for first-year medical students every year for twenty-five consecutive years. His reputation as a lecturer has become legendary, and former students often recall his ability to make what for most of them was the most difficult subject in medical school a unique learning experience and a memorable event in their education. It remains unclear why he was such an unusually electrifying teacher. He never referred to notes; nor can any of his collegues recall that he prepared a lecture in the way most teachers do. But his facts were always correct. He did not pander to the students' desires of the moment, and always exposed them to the most rigorous aspects of the subject at hand. He was able to impart excitement into how new knowledge was discovered and then built upon. Few in his classroom ever complained, as some students are wont to do, about being told of recent research discoveries. He kept the students' attention, and they learned, and learned to enjoy it.

Phil enjoyed being departmental chairman, and although he had the opportunity on several occasions to accept a position as a dean or provost (and later University president), he never did so. He felt that as departmental chairman he could continue his own academic research and teaching, and still effectively assist in development of the University. The record of his activities as chairman shows that this was indeed the case. When he assumed the chairmanship of the Biochemistry Department in 1950, his senior, most distinguished departmental colleague, Hans Neurath, decided to accept the chairmanship of the Biochemistry Department at the University of Washington, Seattle, thereby leaving a faculty of four. By the 1960s the department was to have eighteen faculty members and new space in the Bell Building. Thus, from a small department with limited activities and diversity, Phil developed one of the outstanding research departments of biochemistry in the country, with a reputation for providing outstanding graduate students who came to occupy leading positions in the world of biochemistry.

Phil was also instrumental in developing other disciplines at Duke University. This was largely through his efforts to identify and help recruit promising young scientists to key departmental chairmanships. Noteworthy among those he helped bring to Duke were James B. Wyngaarden, who had a joint appointment in medicine and biochemistry and was then to serve as chairman of the Department of Medicine for fifteen years before becoming director of the National Institutes of Health in 1981. In addition, he was a major force in bringing Daniel C. Tosteson, presently dean of Harvard University School of Medicine, to Duke as chairman of the Department of Physiology and Pharmacology. Wyngaarden and Tosteson, along with many others Phil helped attract to Duke, were key individuals in bringing the School of Medicine to the front rank of American medical schools.

Phil's commitment to excellence in scientific and medical education naturally involved him in design and implementation of new, experimental, educational programs. Perceiving a lack of physicians qualified for careers in biomedical research, he was to develop a research training program for medical students and residents at Duke that gave them not only a concentrated, rigorous education in various fields of basic medical sciences, but also an opportunity to do research under supervision of the best scientists in the University. This program, in effect for about fifteen years until terminated as the result of the shortage of training funds at the

NIH, was to bring a large number of the best young physicians at Duke into research careers. Indeed, graduates of the program are to be found today in many medical schools throughout the country. Phil's perception in the late 1950s of a national shortage of scientifically trained physicians is but one example of his wisdom and farsightedness.

Phil catalyzed the development of other educational and research programs at Duke, not all of which need be mentioned here. Nevertheless, his notions about the role of research in medical education were sufficiently accepted by the Duke faculty to spur the creation of a new curriculum—providing an opportunity to spend a full two years in elective work, including the possibility of at least a year of research—at the School of Medicine in 1967. This curriculum, in slightly modified form, is still in effect today. Of course, he recognized that not all physicians should become researchers, and his remarks in Nashville, Tennessee in 1976, at the dedication of the Harold D. West Basic Medical Sciences Building at Meharry Medical College reveal well his feelings on the role of research in medical education. He said,

> . . . our experience indicates that the best of medical education also occurs within the atmosphere of research. Indeed, those medical students who are not themselves caught up in the research endeaver are, nevertheless, more thoughtful, more analytical, more aware of their own limitations, better prepared for a lifelong medical education and, therefore, more useful as future physicians, when trained in a modern research-conducting medical center.

A description of Phil's academic career would be incomplete without mention of his role as coauthor of the *Principles of Biochemistry*, a textbook designed for medical and graduate students. Planning for the first edition of this text was begun in 1949 by Phil, Abraham White, DeWitt Stetten, and one of us (E. L. S.). Phil was the youngest of the group, only thirty-two, but he already had a reputation as an excellent researcher and an outstanding teacher and expositor of biochemistry. The first edition was five years in writing, and appeared in 1954. The text by White, Handler, Smith, and Stetten was widely adopted, and after Stetten withdrew as coauthor, had seven editions. Phil insisted on collaborating on two revisions, even during his busiest periods as president of the Academy, and regarded his participation as his "lifeline to Biochemistry." In his words, the collaboration was "as rich an experience as one could possibly ask. We have had the enormous joy of a relaxed, harmonious yet intense working relationship conducted with mutual respect and affection. Little more than acquaintances when we began, our ever-deepening friendship has surely been among the best things that happened to any of us." I. Robert Lehman and Robert L. Hill joined White, Handler, and Smith for the sixth edition, and Robert J. Lefkowitz joined the group for the seventh edition, but the spirit Phil helped bring to this endeavor in early editions persisted through to the last, even though Phil, in failing health, was only involved in the early planning.

Contemplating giving up his academic career and personal research in 1969 to become president of the National Academy of Sciences gave Phil much anguish. He was convinced that his effectiveness as science advisor in public life was largely the result of the fact that he was an academic, not a full-time bureaucrat, and were he to give up his life as researcher, teacher, textbook author, and departmental chairman, he would in time lose his effectiveness. Moreover, he feared that he would not be able to resume his former academic career after six years in office, and certainly not at age sixty-two after twelve years, were he to serve for a second term. It is unclear whether he ever overcame completely these fears, but as president of the Academy, he was tenacious in his attempts to stay abreast of his science. We know that he continued to read in various journals, because he often took aback his academic friends when he began to discuss the experimental details and implications for future studies of a paper in the latest issue of a periodical. The only time that one could possibly expect him to have time to read such journals was during the two months or so he spent at Woods Hole each summer. But those who visited him there know that he was still conducting Academy business full time, in addition to all the diversions, scientific and social, at the Marine Biological Laboratories. The historical record will show that Phil's fears of becoming ineffective by giving up academic life were unfounded, but they reflect his deep commitment to academia, its values, standards, and ideals, as well as its way of life.

PUBLIC SERVICE

Recalling some major events in his life, Phil once wrote, "One other turning point in my life should be noted: in 1953 as chairman of the Nominating Committee of the American Society of Biological Chemists (ASBC), Severo Ochoa called me to serve as secretary of the Society. Filled with wonder at this invitation, I accepted. It was this event that turned my face, increasingly, to the organization of science, its role in society, its relationship to government, etc. Ever since I have given at least half of my effort in this direction as will be evident from the accompanying curriculum vitae." Phil was to serve for six years as secretary of the Society, which was but the first of the many national offices he was to hold. He managed all the business of the Society for six years except the editorial affairs, which were handled at that time in New Haven, Connecticut. The annual program of the Society was planned in the teaching laboratory at Duke, where the biochemistry faculty would gather with Phil for a day or two to sort into logical groups the research abstracts for oral presentations, give them session titles, and then choose the chairman of the session. Within a few years of Phil's term in office a full-time executive secretary was needed to manage the business of the Society. Phil was subsequently elected to terms as councillor and then president of the Society. After completion of his term as chairman of the Society's Publications Committee, he had held office in the Society for sixteen consecutive years. The pattern of Phil's public service activities was well-described by his former student and colleague at Duke University, Henry Kamin, who wrote in *Nutrition Today* (March/April, 1982):

> The most remarkable feature of Handler's list of public service accomplishments is the recurrent pattern of appointment to some body, followed by rapid ascent to its chairmanship or presidency. On such bodies Phil's talents became visible almost immediately to his colleagues, and his selection for leadership was easy and almost automatic. It may be well at this point to emphasize that Phil, while totally sophisticated, was not Machiavellian, as may sometimes have been thought by those who observed his success but knew him only superficially. Phil rose in his positions because of a combination of courage, clarity of vision, and remarkable ability to express his thoughts with precision. Since he was altruistic as well as practical, he was always deeply concerned with the objectives of the groups or tasks in which he was involved, and he was always careful—consciously so—of his obligation to strengthen the groups and institutions which he served. It was these qualities of character, thinking, and use of language which propelled him repeatedly to positions of leadership.

In the same year that he was elected secretary of the ASBC, Phil was also appointed to membership on the Biochemistry Study Section of the National Institutes of Health, a group that advised the various Institutes as to the scientific merits of the research grant applications in biochemistry. This was the first of many advisory roles that Phil was to accept for various federal agencies.

In his activities as officer of scientific societies and member of government advisory committees, Phil's abilities as an efficient organizer and administrator and articulate spokesman for science, particularly in its relationship to governmental support, soon became widely recognized. Accordingly, he was to serve as a member of the Board of the Federation of American Societies for Experimental Biology (FASEB), a confederation of six biomedical science societies, including the ASBC, and in 1956 he became chairman of the Board. He was pleased with the decisions he participated in while associated with the Federation, not the least of which was the purchase of the property on Rockville Pike in Bethesda, Maryland, where the permanent offices of FASEB as well as the ASBC are now located. Government advisory groups to which he was appointed in the 1960s included the National Science Board, first as member, then vice-chairman, and finally chairman, and then the President's Science Advisory Committee, on which he served under two presidents.

It was because of Phil's articulate exposition of his faith in the scientific endeavor that he was called upon more and more to explain to congressional committees and the public the importance of basic scientific research, research training, and the benefits that accrue to society. It should be recalled that during this period, in the 1950s and early 1960s, there was an enormous growth in support for research and a strong public interest in its values and benefits. Phil expressed for the scientific establishment its own faith and values. This faith was not merely articulated again and again; Phil was shrewd enough to know that the objectives could be attained only by proper and effective organization and programs.

At the NIH he played a major role in helping to create the various training programs, career development awards for younger scientists, and the National Institute of General Medical Sciences. Needless to say, many others also participated in planning and encouraging these developments, but Phil's role as an effective and patient expositor of these programs to the Congress and others helped enormously. In the same way, he greatly influenced the policies and programs of the National Science Foundation through his service on the National Science Board.

Long before he became president of the Academy, Phil had been called upon to testify before Congress at appropriation hearings for the budgets of the NIH and, later, the National Science Foundation. There was hardly a year in which there weren't several such appearances. Emilio Daddario, a former member of Congress, recalls Phil on these occasions, ". . . called upon to give testimony before numerous of the congressional committees, he became a well-recognized Washington figure with a reputation for both wit and veracity. Beyond that he had the courage to cast aside a carefully prepared script and the temerity to extend into extemporaneous remarks, superlative and spell-binding arguments. As one of the early 'Handler watchers,' I had the chance to see him come into the Washington scene and by a combination of consistency and brilliance become the major spokesman for science."

The last public office Phil was to hold was the presidency of the National Academy of Sciences. He was elected to membership in the Academy in 1964 and was soon active in its affairs. He was a member of the Council from 1966 to 1969 and chairman of the Committee on Life Sciences from 1967 to 1970. An outgrowth of the latter position was his role as editor of the book, *Biology and the Future of Man* (Oxford University Press, 1970), in which an attempt was made to assess the "state of the art" of a given discipline in biology, a summary of recent progress, and the major outstanding questions in that discipline. This book contains a unique summary of the current understanding in the life sciences at the time. Its final chapter is an essay, largely written by Phil, that attempts to analyze the challenges mankind faces in the final decades of the twentieth century. Its message is as meaningful today as it was when it was written.

The nominating committee of the Academy presented Phil as the candidate for president in the fall of 1968. He was honored to have been chosen, and eager to be in office after the annual spring meeting of 1969 when he was duly elected. Having come to grips with himself about leaving academia and a highly satisfying and productive career in research and teaching, he began at age fifty-one his first full-time job as an administrator, but it was a job for which many felt he had been preparing since his first experience on the national scene in 1953.

PRESIDENT OF THE ACADEMY

As Academy president, Phil had a primary role in influencing Academy policy on major issues. Once policies were established, he was the primary spokesman for their announcement and publication. Few scientists have ever been as eloquent as Phil, and he used every possible forum to defend vigorously his or the Academy's position. In the remainder of this section the quotations of Phil's remarks illustrate not only his eloquence, but also his views on several major issues that were to arise during his twelve years in office.

Throughout these years there were those who attacked science itself as well as its technological applications. The following quotations are his statements of defense against such critics.

> Creative scientific research is one of the very purposes of our society akin to imaginative scholarship in the humanities and innovation in the arts.

Surely, no other course available to this civilization is as hopeful as the continuing subtle interplay of science and developing technology.

From "The University in a World in Transition"
The Convocation Address of the One Hundred and Fiftieth Anniversary of the University of Virginia, October 21, 1969

There are those who, equating science with an immoral technology and distrusting our societal leadership, would abandon the scientific quest. But that way lies book-burning. If man cannot learn to live not only with this technology, but with his understanding of himself and his universe, surely all is lost. Inquiry is among man's noblest pursuits.

From "Is Science Relevant?"
A lecture presented at Northwestern University, March 4, 1970

The obligation of scientist remains clear: to pursue science at its frontiers and to address society's problems, including the national defense, where-ever genuinely constructive opportunity affords. Tomorrow, as yesterday, we shall be judged by our success in meeting both sets of challenges. We would be ill advised to offer guarantees of success—we can guarantee only that those challenges will certainly not be met if we are not permitted to try.

From a statement presented to the Subcommittees on Energy Research and Production and on Science Research and Technology, House Committee on Science and Technology hearing on Destinies for American Research, December 10, 1979

Deeply troubling . . . are suggestions that there are questions that should not be asked, that there are fields of research that should be eschewed because mankind cannot live with the answers. Nonsense! No such decision can be rational, much less acceptable. Someone will learn, somewhere, sometime. It is both the glory and the curse of the human brain that we must forever live with truth, once it has been gained. Surely, it is far more dangerous to live with ignorance. . . .

From "Science in a Free Society"
The Phi Beta Kappa Bicentennial Lecture
College of William and Mary, December 6, 1976

The Vietnam War was a troublesome time for the Academy. E. R. Piore, who served as treasurer during most of the time Phil was in office, recalled this period as follows.

The nation's debate on the Vietnam War produced a strong sentiment among some Academy members for the Academy to take a formal position on this national issue. Among the interventionist group were those who, during the initial USA involvement in Vietnam, did advise the Department of Defense on weapon systems. Philip Handler contained the potential fission and prevented it. Naturally the Congressional Charter passed in 1863 and signed by President Lincoln was at stake. The debate (on the USA involvement in Vietnam) and the vote of the members at the annual meeting put the issue to bed. Phil displayed great tact and produced a calm atmosphere throughout. The action of one member had a profound impact on calming the drama. Before the scheduled opening of the annual meeting, a member distributed his letter of resignation from the Academy to the reporters. The press had the letter before it was communicated to the Academy. There was one other resignation; that individual did not indicate the reason for his resignation.

Phil, reflecting on the Vietnam period near the end of his second term in office, wrote,

> Of all that happened, probably most important was my stubborn determination that the trauma and divisiveness of the Vietnam War—which inserted itself so powerfully into the life of the Academy—was not to be permitted to injure, much less destroy the Academy. There were bad days when it felt as if nothing but my own physical body was serving as glue to hold the institution together. There were members willing to sacrifice the Academy for the cause which they held dear—those who filibustered the Business Meeting, misused their positions on the RRC (Report Review Committee), threatened to resign, etc. However right they may have been with respect to their cause, I simply would not allow them to use the Academy as their means of protest, not allow them to fragment the Academy as their issue was fragmenting the country. In the end, the course proved to be correct. Wounds have healed and most have forgotten them.

Often the Academy is perceived by some as a branch of the federal government, and that it must respond if ordered to do so by the executive or legislative branches of government. Phil was extremely sensitive on this issue and was always eager to point out that the Academy was not a part of the government but, as its charter stated, was established to advise the government on request with the option to refuse. E. R. Piore also recalled an occasion when this was a central issue.

This annual meeting raised the issue of the relationship between the National Research Council and the Department of Defense (DoD). The monetary value of the defense contracts was between one to three percent of the total value of contracts with Federal agencies. A procedure was put in place that would make all contracts from the Department of Defense visible to members. The anti-Vietnam mood of the country expressed itself by the passage by Congress of the Mansfield Amendment to the Defense Appropriation Act, and defined the research that Defense is permitted to support. An attempt was made to direct the Academy to pass judgement on whether DoD was complying with the Act. The Mansfield Amendment restricted the type of research the DoD can undertake, and Phil took a strong position on rejecting Mansfield's requests to have the Academy review all DoD research and development programs as to the pertinency to the Department's approved mission. Fortunately, time was available to make Congress understand that they could not direct the Academy and the National Research Council to do anything. Congress can suggest but the Academy and NRC can refuse—this is based on the Academy charter. Thus the Academy was not involved in the exercise of passing judgement on any piece of research and its relation to DoD needs.

Such experience as above put a burden on NRC of following legislation to insure that Congress does not direct the Academy. Currently, Congress asks an agency to consider whether NRC should study a problem, or a set of problems. This procedure provides an opportunity to discuss the proposed investigation, and the NRC can determine whether such study is appropriate for NRC to undertake.

Phil was very much concerned about involving the membership of the Academy in its activities and in keeping them informed. He expanded the use of the *News Report* and inaugurated a series of *Letters to the Members*. New projects and publications were listed, and the various activities were summarized. As he remarked to one of us more than once, "Most of the year, for good or ill, I have to be the Academy.

No one else is here to answer the telephone or the mail. I have to inform the membership." And inform he did.

At each annual business meeting, after the election of new members, he gave a presentation of his view of the state of science and the scientific endeavor, including its governmental and international aspects. These talks became eagerly anticipated by the members and were enthusiastically received, not only for the brilliance and clarity of his exposition, but also for his eloquent and frequently poetic statements of his faith in the values of science, his enthusiasm in its accomplishments, and his pride in the role of the Academy in American life.

Phil was often required to speak before public groups and for better or worse, his remarks often became the position of the Academy. But he was very sensitive about being considered the "high priest" of science, as one reporter once referred to him. Again, E. R. Piore recalls Phil's feelings and behavior in this regard.

> Phil was always concerned with who owns the Academy. It was clear in his mind that the membership were not stockholders, but in effect were agents selected with a special trust on behalf of the nation to serve and advance the integrity and scientific objectives of our nation. This being so, then the quality, the confidence, and the integrity of each of the many boards, committees and panels of NRC, as well as the parent body, the Academy, are the central responsibility of the Academy as a privileged public institution. Members of the Council of the Academy had very heavy responsibilities. Thus one can observe that Phil very seldom used the Executive Committee, and exposed the members of the Council to all the problems, all the concerns that he faced sitting in Washington, concerns that dealt with science policies and the impact of the content of science on government policy.

Phil was very much concerned with the international character of science and actively sought to further the role of the Academy in international affairs. Thus, there were periodic joint meetings involving officers and Council of the NAS and the Royal Society, alternately held in London and

Washington, and with the Soviet Academy in Moscow or Washington. Contacts were maintained with other foreign academies as well. When the opportunity came in 1973 to open scientific relations with The People's Republic of China, he became personally involved. Together with foreign secretaries of the Academy and others, he traveled widely to foster closer international relationships.

Phil played an important role in the establishment in Austria of the International Institute of Applied Systems Analysis. He was particularly skillful in the delicate diplomatic tasks of building this complex consortium and gaining the adherence and support by the major scientific bodies of the U.S.S.R., England, Japan, Germany, and the like. Unfortunately, after his retirement the U.S. government withdrew its financial contribution for the National Academy affiliation and the role of the U.S. has been assumed by the American Academy of Arts and Sciences.

Phil was very much concerned with the freedom of scientists to pursue research, to interact freely with other scientists, and to travel. With the concurrence of the Council of the Academy, a Committee on Human Rights was formed to monitor the treatment of scientists in any country that abused these rights. When Andrei Sakharov, a foreign member of the Academy, was restricted to the city of Gorky, the Academy suspended negotiations on the renewal of scientific exchanges and terminated the ongoing program of bilateral symposia. Yet recognizing the dangers of the arms race, Phil appointed a Committee on International Security and Arms Control, which meets periodically with the corresponding committee of the Soviet Academy.

Phil agonized over the suspension of the joint symposia with the U.S.S.R. and remarked that, "deliberately to limit communications between members of the scientific community is a moral sin," and described the action as "painful and deeply repugnant" and "an ugly precedent." He said that yet it was "the smallest clear signal of the depth of our distress that we could devise."

The Helsinki agreement specified that a scientific group would meet to study its implication as it applied to science and scientists. At the Hamburg meeting, Phil was head of the U.S. delegation and became its major spokesman. Secretary of State Cyrus Vance wrote to him on March 24, 1980: "I want to thank you for your superb performance as head of our delegation to the Scientific Forum of the Conference on Security and Cooperation in Europe. Your negotiating skill and dedication to the advancement of both human rights and scientific cooperation contributed decisively to the successful outcome of the meeting. . . . Your contribution to science is already well known. For your contribution to diplomacy, we all owe you a debt of gratitude."

No account of Phil's presidency should fail to comment on how his tastes and interests left their marks on the Academy. Although his close friends often questioned his taste in art and music, he turned the walls of the Academy building into an art gallery and an art exhibit was continually on display, as it is today. He made the Academy auditorium available for musical and cultural events. One of his favorite events during the annual meetings was the concert just after the garden party on Sunday evenings. He always chose the artists who performed, and members were exposed to his wide range of tastes—from Mozart and Beethoven to Gershwin and Joplin. The night of the concert by the Preservation Hall Band from New Orleans, there was dancing in the great hall, as Phil often recalled with great delight. One member of the Academy said to him then, "You know, Phil, I think this is the greatest evening in the history of the National Academy of Sciences." These concerts, still a major event of the spring meetings, are now called the Lucy and Philip Handler concerts, in recognition of Phil and Lucy's love of them.

Above all, Phil was responsible for the statue of Albert Einstein at the corner of Constitution Avenue and Twenty-second Street. He conceived the idea for the statue, raised funds for it, commissioned the sculptor, and followed in great detail the sculpture itself before and during its construction. There was criticism of the high cost of the Einstein statue, as well as its artistic merits. Phil was very sensitive to such criticism, especially in view of the efforts he made for its success, including fund raising, which he especially disliked. But to Phil, Albert Einstein symbolized the best in science and humanity of our century, and he was delighted when it became a regular stop for tourists, many of whom photographed their children perched at the feet of the great man. Science was brought to Constitution Avenue, the major thoroughfare of our nation's capital, in 1924 with dedication of the present Academy building, but it was Phil who succeeded in bringing a statue of a scientist to stand alongside those other great Americans who are so honored nearby.

Phil, who was the eighteenth president of the Academy, died in Boston on December 29, 1981, of pneumonia, after prolonged suffering from lymphoma, just short of six months after leaving office at the Academy. He never returned to Duke University as he had planned nor was he to leave the hospital after his admission for a thorough checkup in August 1981. He chose that his ashes be placed alongside those of his colleagues at Duke University Medical Center, where he started his academic research career.

WE ARE GREATLY INDEBTED to many friends and colleagues for their help in preparing this memoir. Emanuel Piore was particularly helpful in recalling Phil's role as president of the Academy. For Phil's early years, we have leaned heavily on the autobiographical notes deposited with the Academy at the time of his election; unattributed quotations are from these notes.

CHRONOLOGY OF MAJOR ACTIVITIES AND HONORS

The complete list of Philip Handler's activities, honors, and lectureships is far too long to include in the appended list. The material included here is selective of his major involvements. It should be noted that he received many honorary degrees and presented numerous commencement addresses, talks at various organizations, and the like. He lost no opportunity to present his views on science and society, to defend the principles of intellectual freedom, and to illuminate the beauty of man's accomplishments in his pursuit of scientific truth.

1917	Born, August 13, New York City
1936	B.S., College of the City of New York
1939	Ph.D., University of Illinois

POSITIONS HELD

1937–1939	Junior Chemist, U. S. Regional Soybean Byproducts Laboratory

Duke University School of Medicine:

1939–1942	Fellow and Instructor, Nutrition and Physiology
1942–1945	Assistant Professor of Physiology
1945–1950	Associate Professor of Biochemistry
1950–1961	Professor of Biochemistry and Chairman of the Department
1961–1969	James B. Duke Professor of Biochemistry (on leave 1969–1981) and Chairman of the Department
1969–1981	President, National Academy of Sciences
1970–1981	Distinguished Professor of Medical Sciences, George Washington University

AWARDS AND HONORS

1943	C.B. Mayer Award, New York Academy of Medicine
1964	Member, National Academy of Sciences
1964	Townsend Harris Medal, City College of New York
1966	Annual Orator, Harvey Cushing Society
1966	Fellow, American Academy of Arts and Sciences
1966	Sigma Xi National Lecturer
1969	Annual Award for Distinguished Contributions to Medical Sciences, American Medical Association

1969	Member, American Philosophical Society
1970	Benjamin Franklin Fellow, Royal Society for the Encouragement of Arts, Manufacture and Commerce
1970	Honorary Member, Swiss Academy of Natural Sciences
1972	Alumni Achievement Award, University of Illinois
1972	German Academy of Natural Sciences, Leopoldina
1973	Honorary Member, American Institute of Chemists
1974	Honorary Member, National Academy of Medicine of Mexico
1975	Copernicus Medal, Polish Academy of Sciences
1977	The Great Cross of Honor with Star, Government of Austria
1977	Insignia of Commander of the Order of Leopold II, King of Belgium
1978	Honorary Member, Imperial Iranian Academy of Sciences
1978	Commander, Order of Merit, Peoples Republic of Poland
1979	Distinguished Public Service Award, National Science Foundation
1981	National Medal of Science
1968–1980	Honorary degrees from twenty-seven American Institutions and from the Hebrew University, Israel

PUBLIC SERVICE: ACADEMIC INSTITUTIONS AND SOCIETIES

1953–1965	Federation of American Societies for Experimental Biology, Member of Board (1953–1965); Executive Committee (1959–1965); Chairman (1964–1965)
1953–1968	American Society of Biological Chemists, Secretary (1953–1958); Councillor (1958–1961); President-elect (1961); President (1962); Chairman, Publications Committee (1965–1968)
1967–1981	National Academy of Sciences, Chairman, Committee on the Life Sciences (1967–1970); Councillor (1966–1969); President (1969–1981)
1969–1981	Board of Trustees, Rockefeller University

1973–1979 Board of Trustees, Nutrition Foundation
1974–1981 Board of Governors, Hebrew University of Jerusalem
1981 Board of Governors, Weizmann Institute of Science

PUBLIC SERVICE: GOVERNMENTAL INSTITUTIONS

1952–1962 Consultant, Veteran's Administration
1964–1968 President's Science Advisory Committee
1968–1974 President's Science Advisory Committee
1969–1981 Committee on National Medal of Science
1980 Chairman, U. S. Delegation to the Scientific Forum of the Conference on Security and Cooperation in Europe, Hamburg

National Institutes of Health:

1953–1956 Biochemistry Study Section
1956–1958 Chairman, Biochemistry Study Section
1956–1959 Committee on Health Sciences Training
1958–1961 National Advisory Health Council
1963–1967 National Advisory Council on Research Resources and Facilities

National Science Foundation:

1958–1960 Panel on Biological Research Facilities
1960–1962 Divisional Committee for Biology and Medicine
1962–1974 National Science Board, Member
1964–1966 National Science Board, Vice-Chairman
1966–1970 National Science Board, Chairman

TRIBUTES AND HONORS

At the last meeting of the Academy before his retirement in 1981 from the presidency, Philip Handler was honored by a symposium on biochemical topics presented by four of his former students. After his death, a tribute in the form of a special convocation was held at the Academy on February 8, 1982.

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