1977

Institute to University

The Rockefeller University

PRO · BONO · HUMANI · GENERIS

75

1901 · 1976

INSTITUTE TO UNIVERSITY

A SEVENTY-FIFTH ANNIVERSARY COLLOQUIUM · JUNE 8, 1976

Acknowledgment

The publication of this volume was made possible by a gift from Mr. and Mrs. Carl H. Pforzheimer, Jr.

Library of Congress Catalogue Number 77-24825
ISBN 87470-025-6
Printed in the United States of America

CONTENTS

Foreword

THE HISTORY AND DEVELOPMENT of our institution, in which the alumni have played such an important role, constitute a significant chapter in the history and development of medical science in this country and the world during the past seventy-five years. It is fitting, therefore, that on the first general reunion in our history, we spend some time looking backward at a few of the trends and the personalities that built and maintained this unique university.

In addition, because both research and graduate education are in a period of flux, we will also consider the present and its problems—virtually universal problems—that we are facing today.

Of course, looking at the past and the present reveals only parts of the picture. The third part is the future. Without the extraordinary past and the productive present of the Rockefeller, the future might be bleak because of economic uncertainties. We believe, however, that the strengths of the past combine with the vigor of the present to establish a firm foundation on which we shall build the next seventy-five years. This subject is also addressed in these pages.

We are deeply grateful to Mr. and Mrs. Carl Pforzheimer, whose generosity has made it possible to publish the memories and projections expressed at our reunion on June 8, 1976, and so to share them with friends in this country and abroad.

FREDERICK SEITZ, *President*

I

SIMON FLEXNER AND THE BIRTH OF THE INSTITUTE

My Father, Simon Flexner

JAMES THOMAS FLEXNER

I WAS BORN IN 1908, when The Rockefeller Institute for Medical Research was seven years old. I hesitate to claim that I was conscious of the Institute in my cradle, but as far back as anything registered in my memory, the Institute was there. It was indeed the most pervasive phenomenon, outside of my own personal life, with which I grew up.

I must confess that my childhood attitude toward the Institute was simplistic. I knew that the institution had not existed before my father became the director. I knew that its beginnings had been small, and that under his guidance it had grown great. I knew that he had contributed to that greatness with his own scientific discoveries. He was still at the helm. It was natural for me not to take into adequate consideration the contributions of others.

The Biblical statement that "A prophet is not without honor, save in his own country and in his own house" was not exemplified by my father. I was brought up to revere him as a great man and, as a member of my particular generation, I could do so naturally, without the resentment a child might feel today. All the adults with whom I associated respected my father. The admiration of our German governess for the "Herr Direktor" was indeed so comically extreme that family memory cherished the occasion upon which Fräulein laughed at the great man. While greasing the automobile, my elder brother, suitably named William Welch Flexner, handled his implement—it was known as a grease gun—so carelessly that father was inundated. Responding with fury as grease dripped down his forehead and from his nose, he shouted that William should not be entrusted with dangerous weapons. The proceedings continued in a

spirited vein until they were interrupted by the amazing sound coming from Fräulein's lips. In an instant everyone, including my father, was laughing, too.

The sense of father's greatness was the romance of my childhood. We were not poor, but there were many things I should have liked to have that I was told we could not afford. I remember particularly—those were the days before plastics made toys crude and cheap—that I yearned for a little metal automobile with interior peddles in which a child could go whizzing along. My regret at my deprivation was tinctured with pride when I was told that I could have a dozen such expensive toys if my father were willing to abandon his scientific career to become a consultant whose presence would be considered a necessity whenever a rich person was very ill. The slightest step in that direction would have horrified me.

As I grew older, I became increasingly conscious of my father's gratitude to the Rockefellers for the opportunities they had given and were continuing to give to him. He felt toward the founders, father and son, a very strong sense of loyalty. My parents and the Rockefeller Jrs. were friends, although only my mother's relationship with Mrs. Rockefeller included any intimacy.

The presence of the Institute in my childhood, and particularly the benignity of the presence, had much to do with my mother. She was a true collaborator, discussing with my father his problems, being gravely and helpfully concerned. But she was by no means overwhelmed. Living with a powerful husband, two sons, and a male sexist pig of an Irish terrier, she kept the feminine element afloat with no difficulty whatsoever, partly because my father always treated her not only with love but with respect. Her personal interests were literary. Standing here as a lifelong writer, I need not say how deeply she influenced me.

However, one of the many things about me that concerned my parents was that I was slow in learning to read. It was a family recollection that, when I was goaded, I would state emphatically, "I will not learn to read until I am twenty-one and then I will read the newspaper." Nevertheless, I was worried, too, and it may well have been the greatest triumph of my life when I actually

read to myself a volume dealing with Peter Rabbit. This was an achievement which I felt should not be overlooked, and where could I make a greater splash than in the family center of concern, the Rockefeller Institute?

Father was to make a speech, and as I went to the auditorium—I think it was a room in the Hospital building where movable chairs could be placed—I carried conspicuously my copy of *Peter Rabbit.* I was asked why I had brought the book. Embarrassed to confess that my true objective was a boast, I said that I feared that the speech might be dull and so I had brought along a book to read. This statement achieved, of course, great currency at the Institute as a joke on my father. I hope none of you has brought along a copy of *Peter Rabbit.*

By the time I was old enough to have firm memories and some understanding, the Institute had grown. Although my father was continuing his scientific work—I was awestruck at how many times he washed his hands when he emerged from his laboratory to take me to lunch—much of his time was spent in consultations with the scientists, whom he called his prima donnas. Some, but not many, were intimates of our house. Closest to my father was Peyton Rous, who, with his ebullient wife Marion, seemed members of the family. Dr. Noguchi was always in and out, almost a boy like my brother and me. I remember that after he had given us opera glasses for Christmas, he stood at the far side of the room with his mouth open to see if we could focus on his tonsils. Dr. Carrel, who still exhibited the military crispness of his service in the French army, never stooped to such shenanigans, but had a warm and flattering interest in my father's two sons. Alfred Cohn, who was my father's personal physician, brought into the house what an outsider might have considered a suitably pompous note. Dr. Levene talked about literature and art to everyone's pleasure. Dr. Landsteiner I did not know, but my father pointed him out to me one day on the Institute grounds, and told me to remember the moment, as I was looking at a very great man.

When I reached adulthood and my father was dead, various of the major scientists who had worked with him began to confide in me. I was amazed to have these distinguished men tell me that

they had been afraid of my father, unable to sleep during the nights before they were to have an interview. This made me speculate about myself: had I also been afraid? Certainly, I had formulated no such idea during my childhood, but equally certainly I had, as soon as I was old enough, come to the conclusion that he was not to be crossed lightly—indeed, not to be crossed at all. If I wished to go in some direction of which he might not approve, I was careful to see that he was not concerned or informed. Once, on an idle afternoon, my brother and I, dropping water out of our Madison Avenue window, splashed a lady's fancy hat. She rang the doorbell and left a message with the maid. I remember my intense terror until mother agreed to receive the message and not tell father.

But I knew that we could count on my father's loyalty, as I am sure his associates at the Rockefeller Institute could. This fact cannot be better exemplified than by what could be considered a truly outrageous incident. My uncle, Dr. Abraham Flexner of the Flexner Report fame, was often in our house, where, to my brother's and my outrage, he continually played practical jokes on us and, if we tried to respond in kind, insisted on his untouchability as a distinguished adult. One afternoon he appeared, dressed to the nines, in order to glean admiration before he delivered an important lecture. My brother and I had been working on our skill as pickpockets: we handed people their watches, which they had thought were in their pockets. It was child's play for us to extract Uncle Abe's handkerchief and put in its place a long, greasy rag. He went off blithely to his lecture. In mid-flight, he felt a need to wipe his brow. The result was not what he had foreseen. Shortly after the lecture was over, he came pounding into the Simon Flexner household, demanding condign punishment. Father said to him, "Abe, if you will play practical jokes on my sons, they can play practical jokes on you." There the matter rested.

A favorite family reminiscence, which my father loved to repeat, concerned a stately German scientist who had come to pay a formal call. Father was escorting him to the door of our house when a derby hat came sailing down the stairwell and landed, to the sound of childish laughter, at a crazy angle on

father's head. When he removed the hat with unruffled good humor, the German was doubly taken aback. "America," he exclaimed, "ist das Paradies für children!" Father undoubtedly took pleasure in this anecdote, because his own childhood had been so far from a paradise.

The stories he often told about his early years were always humorous in tone, yet they almost always depicted him as a victim. He told us, for instance, that, after he had hung around yearning to play with some older boys, they had called him in and offered to give him a starring role in one of their games. An egg was to be so expertly hidden that the other boys could not find it. It was sequestered under Simon's hat. But no sooner was it there then one of the boys smashed his hand down on father's head, breaking the egg so that it dripped over his face and clothes.

Sometimes Simon struck back. He had saved pennies that were very hard to come by to procure a particularly lurid dime novel. He was reading happily when his older brother Jacob, who was the tyrant of the family, disapproving of the book, snatched it and threw it into the furnace. Some weeks later, father came on Jacob asleep in his chair. A noiseless trip to the kitchen, a noiseless return with a bottle of ammonia, which he placed under Jacob's nose. As the tyrant sprang up in asphyxiation and then in wrath, father fled and locked himself in the bathroom. We children wondered how he got out safely, but he would carry the story no further.

Although never lacrimose, these reminiscences indicated an unhappy childhood. That a miracle was taking place in the small house in a poor neighborhood of Louisville, Kentucky, was invisible to all the inhabitants, and particularly to my father. His father had emigrated from the neighborhood of Prague and set up as a peddler, carrying hats on his back as he wandered the Kentucky roads. Eventually, he earned enough money to buy a horse, and then he established a wholesale hat store. In the Jewish community of Louisville, he wooed a young woman who had been born in Alsace and had worked for a while as a seamstress in Paris. The couple, as they produced many children, prospered modestly until the business of my father's father was wiped out during the panic of 1873. The father became a clerk in

the hatshop of a former rival, and the sons were sent out to work as soon as they were old enough to earn anything.

Simon was the slow child and eventually the despair of the large family. He could not even finish elementary school without repeating a grade. His formal explanation was that "I was slow in growing up." To me he confided that, as he entered adolescence, he was too disturbed by the presence of the girls to keep his mind on his studies. After he had, at long last, escaped from elementary school at the age of thirteen, an effort was made to find him a job that he could keep. While clerking in a drygoods store, he pulled the chair out from under a particularly pompous and obnoxious customer. He was fired. Surely he could be entrusted with keeping an eye on the enlargements which a photographer was allowing to develop, each for its right number of minutes, in the sunlight! But Simon, who had acquired a jigsaw, forgot time as he drew designs he would cut out of the cigar-box tops and bottoms he could easily procure. So much for that job. He became the chore boy in a drugstore, but now he was writing an epic: *A Dying Arab to His Steed.* Not only did he, as he inscribed his flowing verses, use up quantities of wrapping paper that cost money, but he was too busy with his Muse to sweep the floor. His father felt it necessary to take him for an admonitory visit to the county jail.

The break came when, at the age of sixteen, Simon Flexner almost died of typhoid fever. He rose from the brink of the grave with the ambition, possessed of the energy, direction, and abilities that were to carry him from his inauspicious beginnings to so unforseeable a destiny. He was not to travel alone. Everyone in this room knows that his brother, Abraham Flexner, made as great, although different, a mark on the development of American medicine. And there were other distinguished brothers.

In his new manifestation, Simon Flexner found himself again in a drugstore, but not now as a boy of all work. He was an apprentice. This involved his being sent to a college of pharmacy at night. He brought home a symbol of his changed destiny: the college's gold medal. The medal became a favorite possession of his mother's. She gave it, when my father married, to his bride as the ultimate sign of welcome and renunciation.

Now a graduate pharmacist, my father went to work with his older brother Jacob, who owned a flourishing drugstore. Jacob possessed a microscope, which he used to examine urinary sediments, and the instrument became Simon's obsession. He began by examining random small objects—insect wings and eyes, etc.—but soon he was reading books, teaching himself normal and pathological microscopic anatomy. The local medical profession brought him for examination tissues removed at operations and autopsies.

"The system of the time," my father remembered, was that a drug clerk had "one evening and every other Saturday afternoon free. It was on these evenings at home that I studied or worked most uninterruptedly with the microscope. The domestic picture is still vivid in my mind. The table in the dining room was cleared. My mother sat under the gas-light with a basket of articles to be mended—sewn or darned; the younger children at the table with books and lessons, and I with microscope and its paraphernalia, working away."

Eventually, Flexner went at night to the medical school associated with the University of Louisville. This was the kind of school that his brother Abraham was to put out of business. It was run by the doctors whose prescriptions my father filled during the day. He used to say that he graduated in obstetrics without ever seeing a baby born. "I did not," he later wrote, "learn to practise medicine. Indeed, I cannot say that I was particularly helped by the school. What it did for me was to give me an M.D. degree."

Already he was conscious of the scientific revolution, in the later stages of which he was to make important contributions. At that time, professors, even in major medical schools, were often unwilling to admit that germs could cause disease, but the Kentucky drug clerk had, before he even went to Louisville's humble medical school, read Tyndall's *Essays on the Floating-Matter of the Air, in relation to Putrefaction and Infection.* This book steered him to a life of Pasteur. One of the practitioner-professors at the local medical school gave two lectures on pathology. Discovering to his surprise—he did not yet know much about professors—that the lectures had been cribbed in their entirety from Dr. Prudden's *The Story of Bacteria,* he turned

passionately to the book. How gratified he would have been to know that Dr. Prudden would eventually be a close friend and colleague.

(My own memory of Dr. Prudden was that he lived during the summers on the top of so steep a hill that our Dodge touring car could not get up without boiling over. As the family chauffeurs, my brother and I learned to anticipate the various places beside Dr. Prudden's road where we could find water with which to appease the steaming engine.)

When my father was still working in his brother's drugstore and experimenting with the microscope at home in the evenings, there occurred an event so amazing that, as a seasoned biographer, I should doubt that it had actually taken place were I not confident of my father's truthfulness. A traveler for one of the drug houses appeared sometimes in Louisville and was a trustee of the New York College of Pharmacy. He talked with Flexner and then offered the obscure drug clerk the professorship of pathology at the New York College. But this is not the most amazing aspect of the episode. The obscure drug clerk turned the offer down. Father's explanation was that he realized he did not know enough to accept. But it may be that the youth felt, now that he was moving so fast, drawn toward a different and greater destiny.

Not that he had an exact idea of where he was going. He felt no call toward the practice of medicine. He wished to stick to his books and his microscope, to pathology, to science—but how in that environment, when his weekly salary was still needed at home, was he to achieve so strange an objective? He knew of no place—there was, indeed, in all the United States hardly any place—where a person could make his living by such endeavor. Prophetically, the youth who was to do so much to create the laboratories of The Rockefeller Institute for Medical Research considered founding a one-man laboratory in Louisville. He would back up with scientific studies the local medical practitioners. Perhaps the local medical school would pay him for giving a few lectures annually. Perhaps—he began teaching himself German.

The Flexner family was disentangling itself from its financial

difficulties. Simon's younger brother Abraham had suffered from no such youthful confusion as had retarded Simon. He was a true-blue infant prodigy. There is a story, probably only slightly exaggerated, that he had corresponded with President Eliot of Harvard on the most erudite matters at the age of twelve. He had discovered that a university on the most advanced principles was being founded in Baltimore. Money to go there was forthcoming: the family could only back so shining a light. Abraham graduated in the classics from Johns Hopkins and, soon after his return to Louisville, established a school, also on advanced principles, which prospered, adding more money to the family possibilities.

Word came back to Louisville that the Hopkins was opening, as the first step toward establishing a medical school, a hospital that would admit some graduate students and teach the new scientific medicine—mostly imported from Germany—that was not yet rooted on these shores. Abraham lent Simon enough money to go to the Hopkins for one-half year's term.

The young man, he was now twenty-seven, who appeared at the hospital shortly after it opened its doors seemed in many ways an allegory of the New World seeking in its own way the wisdom of the Old. Although he appeared with the M.D. degree necessary to procure him entrance, he had no formal education to speak of. Almost everything he knew he had taught himself, and in the process he had developed a tremendous hunger for knowledge and an almost Herculean ability to absorb it. With what energy he listened to and took part in the scientific demonstrations; how exhilarated he was by the library full of books that had been unavailable in Louisville; how eager he was to learn everything—codes of behavior and general culture, as well as science—from the more knowing associates with whom he was now thrown! He was observed with wonder and some amusement, and then he made his own small discovery, based on sections of an eye tumor he had brought with him from Louisville to examine when he knew better how to do it. A comet seemed to be starting on its course—but it stopped dead still.

Flexner went to his principal teacher, Dr. William Henry Welch, to announce that he had to go home. Welch said that was

ridiculous. Flexner explained that he had run out of money. "I'll lend you the money," said Welch. Flexner expressed gratitude, but he could not accept the loan; his one term at the Hopkins had already put him too deeply in debt. Welch said, "We have only one fellowship, but it is free for next year. Will you accept it?"

Those words laid a cornerstone on which this great institution was built.

Simon Flexner:
The Evolution of a Career in Medical Science

SAUL BENISON

In 1890, the United States Census reported the close of the American frontier. Three years later, Frederick Jackson Turner, a young historian, mesmerized a meeting of the American Historical Association at the Columbian Exposition with a paper titled, "The Significance of the Frontier in American History." In this paper, Turner suggested that continual efforts by settlers to adapt to the environment of a succession of changing frontiers was not only an important factor in the evolution of democratic society and government in the United States, but was also a key to understanding various admirable features of the American character. Although unspoken, Turner clearly left the impression that, with the close of the frontier, something extraordinary and vital had gone out of American life; in short, that America had lost the magical, phoenixlike quality it had once possessed.[1]

In the very year the frontier closed, a newly minted physician, armed with high hopes and little else, left Louisville, Kentucky, to continue his medical education and training in Baltimore, Maryland. A number of years before, a reigning American seer advised young men about to seek their fame and fortune to "go West." There were not many who could follow Horace Greeley's advice, but it was deemed to be good advice, and was repeated so often that in time it became conventional wisdom. Given the beliefs of the day, the young physician, whose name was Simon Flexner, was clearly traveling in the wrong direction. Worse, he was not even going to one of the great urban centers like New York, Boston, or Philadelphia that had well-established medical schools and hospitals.

In 1890, Baltimore had a population of approximately half-a-

million people. Its streets were but half-paved and, unlike other large cities of the time, continued to rely for drainage on open gutters. There was little virtue in the city. The United States Census piously reported that Baltimore had three times as many brothels as either Philadelphia or Washington.[2] In this unprepossessing urban environment, a group of Baltimore entrepreneurs, aided by an extraordinary educator, Daniel Coit Gilman, and an equally astute Army medical administrator, John Shaw Billings, laid the foundations for a new hospital and medical school. In 1890, that hospital and medical school, named after Johns Hopkins, a Quaker merchant whose philanthropic bequest had helped to found the mother university fourteen years before, was on the verge of training a new generation of students to become physicians and scientific investigators.[3] In microcosm, the evolution of Simon Flexner's medical career at Johns Hopkins and later at the University of Pennsylvania and The Rockefeller Institute for Medical Research, reflects important facets of the development of medical science in the United States at the turn of the twentieth century.

Never did a career in science begin more inauspiciously. When Flexner arrived at the Hopkins in 1890 for postgraduate work in pathology, he discovered that the University of Louisville Medical School had provided him with little more than a diploma. He had a minimal knowledge of physiology and pathology, and his knowledge of bacteriology was limited to a reading of Tyndall's *Floating-Matter of the Air,* as mentioned by Mr. James Flexner.[4] Formal classroom lecture was minimal and initially he foundered. Fortunately, Dr. William T. Councilman[5] took him in hand and, with his help, Flexner began to assist at autopsies. In the year that followed, Flexner became adept in gross anatomy and in the laboratory techniques of preparing pathological slides and specimens, and later became assistant to Dr. William H. Welch, head of the pathology and bacteriology departments. In 1891, when Councilman was working on the pathology of amoebic abscess of the liver, a great deal of fresh surgical material was brought to the pathological laboratory for examination. It fell to Councilman's assistants to search for living amoebae. In his autobiography, Flexner writes, "I took part in this search and thus became acquainted with the particular

species, amoeba histolytica, concerned. The quality of the pus in amoebic abscess was peculiar. Thus, when a specimen of pus from an abscess of the jaw was brought to the laboratory in 1892 I looked for and found amoebae in it."[6] Learning by doing in pathology became the outstanding feature of Flexner's training, and with this and like experience he was able to undertake his first independent investigation in bacteriology in 1892. The problem related to the diphtheria bacillus.

Although Friedrich Loeffler had discovered the diphtheria bacillus in 1884, many physicians in subsequent years would not accept that organism as the sole cause of diphtheria in human beings. Some investigators had difficulty in cultivating the bacillus. Moreover, Loeffler had failed to discover in guinea pigs the characteristic organic lesions found in human beings. Welch, who had previously had controversy with Dr. T. Mitchell Prudden, Professor of Pathology at Columbia's College of Physicians and Surgeons, over the cultivation of diphtheria bacilli, was particularly anxious at the time to discover the nature of the histological changes produced in laboratory animals inoculated with living diphtheria bacilli and diphtheria toxin. Characteristically, he assigned the problem to his young assistant. Setting to work, Flexner was quickly able to demonstrate that the inoculation of rabbits with diphtheria bacilli did, in fact, lead to the production of organic lesions similar to those found in man, and that such lesions were caused equally by a soluble toxin. These findings were significant because they at once strengthened the notion of the etiological relationship of the diphtheria bacillus in human diphtheria and, even more important, advanced the conception that the essential effects were the product of a soluble toxic agent. This work was important on yet another count. It led Flexner to an examination of the problem of toxalbumin intoxication.[7]

During the early nineties, one of the ideas gaining ground in bacteriology was that toxins were the chief weapons of injury employed by bacteria. This theme of bacterial toxalbumins intrigued any number of investigators, including Welch. Flexner, encouraged by the results of his diphtheria investigations, decided to make the problem his own, and undertook to study the effects of toxic products of various bacteria, as well as the corresponding toxins of castor and paternoster beans—ricin and

abrin—in rabbits. In time, through his research, he was able to supply a histological basis for this developing bacteriological idea and simultaneously to demonstrate that histological criteria did not necessarily exist for each kind of toxin. Although the results of Flexner's investigation were substantive, it is noteworthy that during the course of this research he observed, but overlooked the importance of, the striking biological phenomenon of anaphylaxis. In 1909, when Dr. Charles Richet of France explained the significance of the anaphylactic reaction, he received a Nobel Prize.[8]

So rapid was Flexner's development as a pathologist and bacteriologist that, when Councilman was called to Harvard in 1892, Dr. Welch appointed Flexner as an associate professor of pathology in his place. Welch demonstrated his confidence in Flexner's abilities in other ways, as well. In 1893, when an epidemic of cerebrospinal meningitis broke out in the Lonacoming Valley in Maryland, Welch, in response to a request for aid from the governor, dispatched Flexner and Dr. Lewellys Barker to investigate the epidemic. While Barker occupied himself with clinical problems, Flexner began a pathological investigation of the epidemic's most recent victims. In the course of this work, he isolated a meningococcus. Although Flexner knew that Dr. Anton Weichselbaum in Germany had isolated a meningococcus in similar circumstances several years before, he mistakenly assigned the diplococcus he had discovered to the class of pneumococci.[9] Dr. Peyton Rous, in a sketch of Dr. Flexner's life for the Royal Society of London, has suggested that the error was made because Flexner could get no laboratory proof for an in vitro cultivation of meningococcus.[10] Rous's suggestion has much merit. Flexner's diary notes show that his laboratory had been set up in a stable under miserable sanitary conditions and that, during the course of his investigations, his Petri dishes had become so contaminated with hay bacilli it was almost impossible to accomplish an in vitro cultivation of the fastidious meningococcus. There were, however, other reasons why Flexner was deflected from drawing the correct conclusions from his initial isolation of meningococcus. Not the least of these was his deference at the time to authority—the authority of position and

the authority that scientific activity itself sometimes inadvertently creates.

Although Flexner knew of Weichselbaum's isolation of meningococcus, he was also aware that Dr. Jacob Baumgarten, one of the leaders of German pathology, had been particularly critical of Weichselbaum's findings. Dr. Baumgarten, then in the midst of debate in German medical journals with Elie Metchnikoff over the role of phagocytes in immunity, enjoyed an excellent public reputation. In the face of his essentially negative laboratory findings, Flexner found it easier to side with the older authority than to try to confirm the work of the younger Weichselbaum. Perhaps the balance was tipped by the very work that the department of pathology at the Hopkins was then engaged in. In the weeks preceding the epidemic, Dr. Welch had lectured extensively on pneumonia. Flexner, as Welch's chief associate, had been particularly absorbed in preparing pathological slides and specimens for Welch's lectures. Given these circumstances, it is understandable why, in an uncritical moment, he could classify the diplococcus he had isolated as belonging to a group of pneumococci.[11] To be sure, an error had been made, but it was the error of a young worker. It is equally plain that Flexner's experience in Maryland added to his developing skill as a pathologist. It was to enhance these growing skills that, later that year, Welch arranged for Flexner to have a period of formal study in Europe with such masters of pathology and bacteriology as Friedrich von Recklinghausen and Karl Weigert.[12]

In the years that followed, as Dr. Flexner's work in pathology developed, he became less concerned with the pathological changes that occurred in organs as a result of disease than in seeking out the nature and the causes of disease itself. When such opportunities presented themselves he grasped at them, even though they might be outside his immediate experience and ability. In this way he came to do his earliest work in pathological chemistry. While performing an autopsy on a case of acute pancreatitis in 1897, Flexner was struck by the existence of areas of fat necrosis in the fatty tissues of the abdomen. He suspected that the lesions might be related to the existence of a fat-splitting ferment secreted by the pancreas. Unfortunately, at

that time he lacked the chemical techniques necessary to undertake a meaningful investigation of his suspicion. Undaunted, he sought help from Dr. John Abel of the pharmacology department. Abel, a superb chemist who, two years later, was to succeed in isolating epinephrine, supplied Flexner with the necessary chemical techniques to carry his work forward. Thus armed, Flexner succeeded in demonstrating the presence of the ferment. Later, he confirmed his findings by producing fat necrosis experimentally in laboratory animals.[13]

In 1898, just eight years after coming to the Hopkins for training in pathology, Flexner was appointed Professor of Pathological Anatomy. In spite of his appointment, he realized that the time had come for him to move. His position was, in essence, that of assistant to Welch. Although he was fully ready to take command of his own department, he had little hope of succeeding Welch, who was then only fifty years of age and at the height of his powers. Even if there had been such an opportunity, the policy of the medical school militated against such an appointment, since it was distinctly organized on the principle of seeding promising young medical-school men in other institutions. In 1899, as offers of professorships from the University of Buffalo Medical School, the Jefferson Medical College, and the Cornell Medical School came in, Flexner began to consider them seriously. Initially, he was disposed to accept the offer made by Cornell; however, when the chair of pathology at the University of Pennsylvania Medical School became available, he accepted it. He later explained to interested friends that he chose the University of Pennsylvania because he believed it offered more opportunity. He pointed out that, unlike Cornell at the time, the medical school at Pennsylvania was an integral part of the university and possessed a full preclinical faculty.[14]

There are indications that, when Flexner arrived in Philadelphia in 1900, the University of Pennsylvania Medical School was not yet prepared to engage in experimental pathology. Flexner discovered that the laboratory facilities which had been prepared for him were inadequate for experimental purposes. Worse, the relationship which had previously existed between the medical school and the pathology service of the Blockley Hospital, on which Flexner anticipated depending for a

steady supply of pathologic material, had been allowed to lapse. In the beginning, therefore, Flexner devoted himself almost exclusively to teaching. Soon, however, circumstances furnished him with an opportunity to engage in an investigation which did much to demonstrate to medical-school authorities the usefulness of scientific investigations.[15]

In 1900, plague appeared in San Francisco's Chinatown. Although the nature of the outbreak was quickly established by Dr. Joseph Kinyoun of the U.S. Marine and Hospital Service, local businessmen and state health authorities proved reluctant to admit the existence of the disease. To complicate matters, a sharp struggle ensued between federal and state authorities over who had the ultimate right to fight the disease. Recognizing the growing public-health menace of the outbreak, the U.S. Secretary of the Treasury appointed Dr. Flexner, Dr. Lewellys Barker, and Dr. Friedrich Novy as a special commission to conduct an independent investigation of the outbreak. Despite roadblocks erected by the governor and the state legislature of California, Flexner and his companions carried out their mandate with dispatch and confirmed Dr. Kinyoun's original diagnosis. Later, as a result of the commission's report, the governor of California modified the state's position and finally requested the federal government to assume responsibility for all plague control work in San Francisco.[16]

Flexner's work on the plague commission provided important, if immediately intangible, personal benefits, as well. In particular, he gained inestimable experience in the politics attending the resolution of public-health problems. More importantly, he returned to the University of Pennsylvania with an enhanced reputation—a condition which was to prove helpful to him in meeting the future problems of the pathology department.

By the end of Dr. Flexner's first year in Philadelphia, a number of problems which had initially hampered his undertaking experimental work began to disappear. First, additional laboratory space was made available to him in the Ayer Laboratories. Second, and equally important, steps were taken to re-establish the relationship between the pathology service of the Blockley Hospital and the medical school. Best of all, a new city adminis-

tration in Philadelphia pushed through an ordinance which permitted autopsies to be performed on all patients who died at Blockley Hospital or the Almshouse. All of these factors combined to increase the scope of the work of the pathology department, and soon a number of young investigators and physicians came to assist and work with Flexner. Among them were Dr. Richard Pearce, Dr. Frederick Gay, Dr. Henry Bunting, Dr. Warfield Longcope, and Dr. Hideyo Noguchi. Throughout his tenure at Pennsylvania, Flexner was absorbed by problems in immunology. Indeed, experimental work in immunology became one of the hallmarks of his department. It served to improve his standing within the medical faculty and won the increasing respect of pathologists and bacteriologists throughout this country and abroad. One measure of that respect is found in the fact that many of the men who worked with Flexner during this period were later welcomed for advanced training by major laboratories in the United States and Europe.[17]

An important turning point in Dr. Flexner's career occurred in 1902, when he was invited to join with William H. Welch, Theobald Smith, Christian A. Herter, L. Emmett Holt, T. Mitchell Prudden, and Herman M. Biggs in planning the organization of The Rockefeller Institute for Medical Research. It is noteworthy that the idea for the Institute, which later was to have such a profound effect on the development of medicine and medical science in the United States, did not originate with a physician or a scientist, but with a layman—Frederick T. Gates, the remarkable Baptist minister who served as business and philanthropic adviser to John D. Rockefeller, Sr.

Gates's interest in medicine was no idle curiosity brought on by his work as Mr. Rockefeller's almoner. It was, on the contrary, long-term and deeply rooted. In part, it was evoked by the experience of his early ministry, which daily brought him to the sick-beds of his parishioners. Equally, it was nourished by his skepticism of the value of the medicine he saw practiced beside these same sick-beds. In 1897, Gates, eager to learn more about the latest developments of medicine and medical practice, undertook to read Dr. William Osler's *Principles and Practice of Medicine*. For five years previously, Osler's text had served as handbook to a new generation of medical students making their

first forays into clinical medicine. In Gates's hands, Osler became a guide for employing Mr. Rockefeller's benefactions in the field of medicine. In the months following his reading of Osler, Gates carefully nurtured the idea of a medical research institute until it took root with Mr. Rockefeller. Originally, Gates hoped to tie his planned institute to the University of Chicago; however, in 1898 the University associated itself with the Rush Medical College, a school which was then not held in very high regard by either Gates or Rockefeller, so that plan was discarded in favor of establishing an independent research institute.[18] In 1901, as a step in that direction, The Rockefeller Institute for Medical Research was certified by the State of New York. According to 1908 revisions in its charter, the Institute was authorized

> . . . to conduct, assist and encourage investigations in the sciences and arts of hygiene, medicine and surgery, and allied subjects, in the nature and causes of disease and the methods of its prevention and treatment, and to make knowledge relating to these various subjects available for the protection of the health of the public and the improved treatment of disease and injury.[19]

If the charter of the Institute, in the manner of corporate documents everywhere, proclaimed the possibilities of future activity, Mr. Rockefeller's original gift of $200,000 was more modest and attuned to a different reality. It was certainly not designed to build an institute immediately. In actuality, it was given for the purpose of securing information on the strength of the existing pool of scientifically trained medical workers, as well as to examine the advisability of establishing such an institute.[20]

To breathe life into Gates's plans, the Board of Scientific Directors charged with planning the organization of the Institute decided that the time had come to appoint a director, and offered the post to Dr. Theobald Smith, the distinguished animal pathologist and bacteriologist. Smith, fearing that his own interests in animal pathology might in the future unwittingly restrict the activities of the Institute, refused the post.[21] The Board, thereupon, offered the directorship to Flexner. It is no secret that this offer was made on the strong recommendation of Welch, who long had had a high regard for the abilities of his old pupil. Less well known are the qualms Flexner had in accepting

the offer. In his autobiography, Flexner suggests one of the reasons for his trepidations and gives, at the same time, a self-portrait of his qualifications and achievements as a scientist.

> My training had been highly unconventional. I need not elaborate this statement which is based on the whole story of my inadequate education. However, I fitted into the educational setup at the turn of the century in a rough and ready way; such a choice as director of a research institution in medicine would be impossible today. Despite the great gaps in my knowledge of medicine of the day I had found that I could work effectively in the pathology and bacteriology of the period, and undoubtedly my conduct of the pathological had brought out certain personal qualifications which Dr. Welch must have believed made my choice a fairly safe one. My own notion is that the way the department of pathology developed in the few years of my professorship at the University of Pennsylvania played a leading part in convincing the scientific directors who knew little of me personally.[22]

Personal considerations, however, were not the only reasons for Flexner's qualms. Others were equally compelling, not the least of which was the state of medical research.

In 1900, medical research was a new, almost unique activity in the United States. Although research was then in progress in such medical schools as Johns Hopkins, the University of Pennsylvania, and Harvard, the vast majority of medical schools did not engage in such practice. Moreover, where medical research was carried on, it was almost always conducted as part of the teaching process. When Dr. Flexner accepted the directorship of The Rockefeller Institute for Medical Research in 1903, noone could foretell whether a pure medical research institute could survive in the United States. Actually, Flexner had no assurances that his new post would be permanent. Although Welch's private assertions to him that "Mr. Rockefeller never deserted anyone" were persuasive, the only sure knowledge that Flexner possessed was that Frederick Gates, Mr. Rockefeller's most trusted financial adviser, was wholeheartedly committed to the idea of a research institute. Flexner didn't even know whether he would be able to assemble and maintain a research staff.[23]

There can be little doubt that existing institutes for medical research in Europe, such as the Pasteur Institute, the Institute für

Infectionskrankheiten, Robert Koch, and the Königlich Preussiches Institute für Experimentelle Therapie, provided a strong stimulus to Flexner and the Board of Scientific Directors in their planning for the Institute. It is equally true that Flexner's vision of a medical research institute differed from the models provided by the European experience in a number of significant ways. In Flexner's view, European institutes of medical research were either created for, or built around, outstanding personalities in medical science, and as such ultimately developed into instruments for extending either the work or the personalities of their directors. For Flexner, The Rockefeller Institute for Medical Research had to look forward to a broader plan of development than one founded on an extraordinary scientific personality. It is of interest that Flexner, who was brought up in the then-rapidly developing sciences of experimental pathology and bacteriology, did not regard bacteriology, which was the cornerstone of European institutes, as being central to the development of the new Institute. This is not to say that Flexner overlooked the continuing importance of bacteriology in the growth of medical science. Rather, his observations of the development of bacteriology, pathology, and physiology had convinced him that those sciences were beginning to draw more and more vitally on the new knowledge being derived from fundamental discoveries in chemistry, physics, and experimental biology. In Flexner's judgment, therefore, if the Institute was to have an optimum development in medical research, it required chemistry, physics, and experimental biology as a cornerstone.[24]

There was an important corollary to Flexner's views, an addendum which, in future, was to differentiate further the Institute from medical schools and universities in which medical research was also carried on. Although Flexner understood the value and need for formal teaching, it was not an activity he saw as essential to the development and growth of the Institute. Indeed, he believed that language requirements, which were necessary for carrying on formal teaching, would function as a bar in acquiring needed investigators who might not be able to speak English. Essentially, Flexner saw the Institute as an organization that could pursue or neglect important fields of research at will. In his own words, "an institution of research as such is built

not about subjects, but about men. Hence, it is in the fullest sense an institution in which opportunism in the best sense of the word plays a determining role." [25]

When the Institute began its operations in 1904, the staff, in addition to Dr. Flexner, consisted of five people: Dr. Samuel J. Meltzer, Dr. Phoebus A. Levene, Dr. Eugene L. Opie, Dr. Hideyo Noguchi, and Dr. Joshua E. Sweet. This staff, recruited by Dr. Flexner, reflected his vision of the Institute. Although all possessed the M.D. degree, all were primarily investigators capable of conducting research in one or more of the basic sciences.[26]

In 1910, two important additions were made. The first reflected Flexner's view of the importance of recruiting superior investigators in the basic sciences, and the second helped define principles of investigative governance at the Institute.

First, Dr. Jacques Loeb was appointed director of a new division of experimental biology (later general physiology) in the department of laboratories—its function to conduct investigations of the physical and chemical constitution of living matter. The work of this division, which began with studies of the effect of salts on cells, developed so rapidly that within little more than a decade Dr. Loeb and his associates had progressed to studies which included, among others, research into the physical and chemical behavior of proteins and the chemical structure of enzymes, handsomely substantiating the director's convictions of the growing importance of chemistry and physics in the development of physiology.[27]

Second, the Hospital of the Institute was opened. Although as early as 1908 the Hospital had been planned as an addition to the Institute, it took the better part of two years for Dr. Rufus Cole, the Hospital director, and Dr. Flexner to reach an agreement as to the research role of physicians in the new facility. There was no previous experience which Flexner or Cole could draw upon, since none of the European medical research institutes contained a hospital. Briefly, Flexner expected the Hospital to act as a testing ground for ideas generated by investigators in the department of laboratories. Cole, on the other hand, felt that if medicine were to advance, the physical and intellectual barriers that separated the ward from the laboratory had to be breached. Accordingly, he argued that special laboratories be developed in

the Hospital, so that physicians might undertake clinical, as well as experimental, research. In a conciliatory move, he agreed that, if members of the department of laboratories needed the use of Hospital wards for the study of cases of the diseases they were investigating, they would be afforded the use of the Hospital facilities. Cole's views were ultimately accepted.[28]

It is to Flexner's credit that, once he reached agreement with Cole, he adhered to it. Indeed, on one occasion soon after, he stretched the agreement to accommodate Dr. Cole. From its inception, one of the unwritten rules of the Institute was that no investigator would knowingly impinge on a problem or an area of research another had previously made his own. Nevertheless, when, early in the summer of 1911, Cole thought it would be important for three of his young residents to engage in a clinical investigation of polio, Flexner not only encouraged that study; he helped perform the autopsies the study required, although polio was clearly his research preserve. In 1912, three residents—Francis Peabody, George Draper, and Alphonse Dochez—published the results of the study as Rockefeller Institute Monograph #4. That monograph remained the Bible on the clinical aspects of polio for the next three decades.[29]

Flexner had little trouble in recruiting senior investigators, but recruiting junior staff proved difficult at times. In 1907, for example, Dr. Dochez, then a recent graduate of The Johns Hopkins Medical School, applied to the Institute for a post in Eugene Opie's laboratory. Unfortunately, the prospects described by Opie proved a disappointment to Dochez, and when Opie offered him the job, he refused. Dochez, reminiscing about the incident almost fifty years later, said:

> Opie then said to me, "All right, go down and see Dr. Flexner. He will arrange for your expenses."
>
> I went to see Dr. Flexner, and Dr. Flexner asked me, at once, whether I was coming.
>
> I said no, that I had decided not to come to the Rockefeller Institute.
>
> He may have said some other things, I don't remember, but one thing that he said stands out very prominently in my mind. He made on his leg the gesture of percussion which the clinician uses, and he asked me, "Are you afraid that you'll forget to go like this?"[30]

Several days later, Dochez reconsidered his refusal and, with Dr. Welch's help, reapplied for the post and was accepted.

For the next three years, Dochez worked with Opie on proteolytic enzymes of the liver and pancreas. In 1910, however, he found himself without a post when Opie left the Institute for a professorship in pathology at Washington University Medical School in St. Louis.[31] This time, Flexner himself came to Dochez's aid with two offers: one, a job in his own laboratory; second, a post with Dr. Meltzer in the department of physiology. Dochez's reminiscences about the dilemma these choices presented reveal in part the awe with which he regarded Flexner.

> I wasn't very anxious to take either of them. I didn't want to take a position with Dr. Meltzer because I knew the men who were working in his department and I didn't think that I'd be interested in doing the kind of work that they were doing, which was largely pharmacological. I had the greatest admiration and respect for Dr. Flexner, and the greatest appreciation of the work that he was doing, because I considered it the most important work, perhaps, that was going on in the Rockefeller Institute. But I was afraid of Dr. Flexner, and I thought, "If I work in his laboratory and he's there this fear will have a tremendous inhibiting effect on my feeling. I'll be afraid to say what I think or try to do what I want to do. If he says anything I'll be completely discouraged." So I didn't want to go with him.[32]

Ultimately, Flexner, with Cole's help, created a special post for Dochez as bacteriologist to the Hospital.[33]

Flexner's efforts in Dochez's behalf were not unique. He often extended himself to forward the professional careers of junior members of the staff. Thus, in 1918, when the British Crown Colony of Hong Kong appealed to the Institute for help in combatting a meningitis epidemic, Flexner chose the unlikely, timid, and gentle Peter Olitsky as the Institute's representative, not only because Olitsky had previously worked on perfecting the Institute's antimeningitis serum, but also because Flexner perceived the occasion as an opportunity for expanding Olitsky's experience and horizons.[34] In 1920, after Walter A. Jacobs, Michael Heidelberger, Wade H. Brown, and Louise Pearce had worked for several years on the chemotherapy of trypanosomiasis, Dr. Pearce, then one of the talented junior staff of the Institute, was chosen by Flexner to go to the Congo to test the

efficacy of the newly perfected tryparsamide. It was a dangerous assignment, but one Flexner was confident Dr. Pearce could carry out.[35]

Perhaps a word should be said here of Flexner's attitude toward employment of women at the Institute. During his tenure as director, twenty-two women were hired as investigators in various laboratories, including his own. It has been argued by some that, although women found it easy to be hired as assistants and associates, few advanced to full membership. While it is true that only Florence Sabin achieved full membership during Flexner's directorship, that was less a reflection of Flexner's attitude toward women investigators than it was of Institute policy of promotion to the rank of full member.

Full membership under Flexner was a prize that was won with great difficulty, and even talented investigators who were associate members for several years were frequently encouraged to seek other posts. In 1920, Dr. John Auer, an associate member and the pride of Samuel Meltzer's laboratory (indeed, his son-in-law), was encouraged to accept a post at the Washington University Medical School, because Flexner did not believe he had the capacity for development as a division chief in Meltzer's place.[36] In sum, in order to become a member one not only had to have an excellent record as an investigator; one also had to give promise of future achievement, and last, but certainly not least, have enough brass or self-belief to fight for the prize. Tom Rivers's account of his promotion to full membership is a case in point.

In 1927, Rivers, who had recently been promoted to a second term of three years as associate member, was offered the chairmanship of the department of pediatrics at Yale University Medical School, and went to consult with Dr. Flexner about the offer. The following is a portion of his account of that consultation.

> . . . Well, Flexner talked to me for about a half an hour about how well I had done at the Rockefeller Institute in the previous five years, and what a bright future I had ahead of me at the Institute if I kept on doing as well in the future as I had done in the past. He was extremely nice.
>
> After he'd talked to me about a half hour, he stood up. We all

knew that, when Dr. Flexner stood up, it meant that the interview was over. I got up and said good-bye to him. I got over to the door, turned the door knob, and was just getting ready to pull the door open, when Dr. Flexner said, "Come back here, Rivers. Come back here, Rivers. You haven't told me what you are going to do."

I said, "Well, Dr. Flexner, you didn't ask me what I was going to do."

He said, "I'm asking you now."

I said, "All right, I'll tell you. If I'm not made a member of the Rockefeller Institute, I'm going to Yale. You say I'm good, that I know how to do research, and that I've got a good future at the Institute, but you've only offered me security for three years. The boys at Yale don't know whether I can teach pediatrics or not, because I have never had a teaching job. They're gambling on me. I may be a bum teacher, I may run a rotten department of pediatrics, but they're giving me $4000 a year more than you are, and security for life, and you ain't giving me anything except a promise!"

I said, "If I am not made a member, I am going to Yale."

He said, "Well, look, Rivers, I can't do anything about it now, the board has already met."

I said, "Dr. Flexner, did you ever hear of the telegraph office? All the people on the board know me. You can get an answer as to whether or not they want me as a member of the Rockefeller Institute very quickly. If you don't make me a member of the Rockefeller Institute before Friday morning, I'm going to Yale." And I walked out of the office.

I didn't hear anything more, but Friday morning, when I got to my office, Edric Smith, the business manager of the Rockefeller Institute, was sitting in my office waiting to tell me that I'd been made a member of the Rockefeller Institute.[37]

Rivers was a unique man who probably would have reached the top in any system of promotion.

In 1939, Dr. Herbert Gasser, who succeeded Flexner as director, confessed to the Board of Scientific Directors that the Institute's promotion policy needed to be revised. Ironically, the necessity of revision was made manifest by the success of the junior members of the Institute. After recounting the extraordinary achievements of then-associates and associate members such as Albert Sabin, René Dubos, Richard Shope, Frank Horsfall, Wendell Stanley, and Philip McMaster, Gasser told the Board:

> Even this brief sketch is enough to show that there is a great aggregation of strength in the junior membership—a strength which is all the more noteworthy because of the small size of the group. There are only six Associate Members in New York. The range of abilities clearly comes up and at its upper end overlaps that of the Membership. In due course, some of the group will undoubtedly be made Members, but certainly not all. . . . Herein lies the source of the need for a change of policy. Not only does the Institute not want to put pressure upon those for whom Membership is not imminent to find new institutional connections, but it has every reason for wanting to hold them in the face of offers made from the outside. In order to conserve its strength, the practice with respect to the tenure of Associate Members can well be made less rigorous. And it may be necessary to create Memberships on a far less elaborate scale than that upon which any have been created in the past.[38]

The policy of promotion to full membership was not immediately modified. Such changes as were ultimately made came under stress of competition for Institute manpower in the period following World War II, when universities and medical schools began to engage in large-scale medical research.

It has sometimes been overlooked that, throughout Flexner's tenure at the Institute, he not only served as director but as an active investigator, as well. Indeed, one of the sources of his strength as director lay in this latter fact. Flexner's achievements as an investigator are perhaps best seen in his research on poliomyelitis.

In 1907, soon after developing an antiserum for cerebrospinal meningitis,[39] Flexner was invited by the New York Academy of Medicine and the New York Neurological Society to join them in an investigation of polio. He was then forty-four years of age. It is of interest that the first important breakthrough in polio research did not occur in the United States, but rather in Vienna. In the fall of 1908, Dr. Karl Landsteiner, then prosector of the Wilhelminen Spital, successfully transmitted polio from a human victim to monkeys. Unfortunately, Landsteiner's achievement was but half a success, for when he tried to pass the disease to other monkeys, he failed. A year later, Flexner followed Landsteiner's lead, and not only succeeded in transferring polio from humans to monkeys, but from monkey to monkey, as well, thus demonstrating what many physicians had long suspected but

had been unable to prove—that polio is an infectious disease. Within months of this discovery, Flexner was also able to show that the organism that caused polio was neither a bacterium nor a protozoan, but rather a virus—then defined merely as an ultramicroscopic organism that could pass through the filters generally used in laboratories to hold back bacteria.[40]

During the spring and summer of 1910, some of the experiments Flexner conducted suggested that the portal of entry and exit of poliovirus in man was through the olfactory pathway.[41] Three years later, Flexner and Noguchi announced in the *Journal of Experimental Medicine* that they had cultivated poliovirus on artificial media, and that when such media were stained, the virus appeared as a "globoid body." They further maintained that when cultures containing globoid bodies were inoculated into monkeys, the animals came down with poliomyelitis.[42] To many at the time, it appeared that the polio problem was on the verge of solution. Dr. William Keen, the doyen of surgery in the United States, was so excited by the prospects opened by Flexner's polio investigations that he nominated Flexner for a Nobel Prize.[43] For the next quarter of a century, Flexner's findings on the portal of entry of poliovirus in man and the globoid bodies helped guide polio research in the United States. In the end, however, these particular findings proved to be wrong.

Many of the polio investigations which were undertaken during the first three decades of the twentieth century were often sustained by Flexner's help in supplying the necessary infectious material and/or advice on experimental technique to carry the research forward. His cooperation and encouragement of young investigators were proverbial. In 1910, when Dr. Robert Osgood, whom Flexner had previously helped, wrote to inquire whether his then own promising research would impinge on Flexner's,[44] Flexner replied:

> I consider the investigation of polio so important that I should welcome any further discoveries you might make as I welcome this one. You should feel free to carry on your investigations in any line where you think it possible to succeed. We cannot, all of us working together clear up this matter too soon.[45]

However, when circumstance required that Flexner act as

critic, he could be harsh, even with people he admired, as an incident in his relations with Dr. Samuel Meltzer reveals.

During the polio epidemic of 1916 in New York City, Meltzer, who several years before had succeeded in briefly prolonging the lives of poliovirus-infected monkeys by injecting adrenalin into their spinal cords, decided to conduct like experiments with polio victims suffering acute respiratory distress. Flexner thought little of the experiment or of the hospital personnel in the East 57th Street hospital who were aiding Meltzer, and wrote a sharply critical letter expressing his disappointment and displeasure over the experiments. Meltzer, who was neither timid or shy, savaged Flexner by return mail and then refused to speak to him.[46] Flexner revered Meltzer as he revered Loeb, and there can be no doubt that he was hurt and troubled by Meltzer's refusal to talk to him. The triumph of getting Meltzer to speak to him again is revealed in a letter that Flexner wrote to his wife Helen several months after the incident occurred.

> . . . The ice is broken with Meltzer it worked out very well. He came to see me while I was talking with Loeb, and so the first anxious moments were got over in his presence. The old man held his back very straight. He looks badly. I then invited him into my office and although he said he came only to report I got him in and soon we were talking in the old style. . . . Not a word about the summer. That can come next time. He left with almost normal actions. So far then so good.[47]

As an authority, Flexner helped establish exacting standards for conducting and interpreting experimental investigations in polio. Meltzer was but one of a long list of investigators working on the polio problem who were subjected to Flexner's searching criticism. Although Flexner reigned as an authority, he was not an authoritarian. He, no less than others, was also subject to the standards he had established. In 1926, in a speech before The Society of American Bacteriologists, Tom Rivers publicly attacked Flexner's theory of growing poliovirus in lifeless media. Here is Rivers's account of Flexner's reaction to that criticism.

> Before I went down to Philadelphia, I made an appointment to see Dr. Flexner to show him my paper. I did this because I didn't think that it was proper for me to speak against the views of my boss, without letting him know ahead of time that I was going to do so.

After he finished reading it, I asked him if he thought it was right or wrong, or if he had any objections to my making the speech. Dr. Flexner looked me square in the eye—and I think that the old boy was sincere. "Rivers," he said, "every man has a right to his own opinion." He didn't say that he agreed or disagreed with me; all he said was, "Every man has a right to his own opinion," meaning that I could go ahead, and I did. I could never tell whether the old guy—and he was a smart old devil—had his tongue in cheek or not. He certainly gave me every opportunity to do what I wanted to do. Whether he believed what I believed, I don't know."[48]

In 1939, when Dr. Albert Sabin, then a young associate at the Institute, demonstrated beyond cavil that the olfactory pathway was not the portal of entry of poliovirus in man, Flexner wrote Sabin a letter commending him on the care and meticulousness of his research. Indeed, that letter illuminates a facet of his contribution to polio research that is all-too-often overlooked.[49]

As director of The Rockefeller Institute for Medical Research, Flexner had the prescience to see the burgeoning importance of viruses as a field of research, and throughout the 1920s and early 1930s he fostered such research at the Institute. Upon his retirement in 1935, virus research was not only established in the laboratories, but in the Hospital of the Institute and the division of animal and plant pathology, as well. It was perhaps fitting that, in the year of Flexner's retirement, Dr. Wendell Stanley in the division of animal and plant pathology announced that he had successfully crystallized tobacco mosaic virus. From that moment, problems in virology were no longer exclusively in pathology, and investigators could now address themselves to problems of the structure and constitution of the virus itself. Flexner lived to see the new land of Canaan; he never entered it. In time, the men whose careers he had nurtured—the Riverses, Shopeses, Stanleys, Coxes, Francises, and Sabinses—would play fundamental roles in the conquest of polio, as well as of other virus diseases.

Epilogue

How does one explain Simon Flexner's extraordinary career in medical science? Apart from his undoubted native ability, perhaps time was the key element in Flexner's development as a bacteriologist and pathologist. He received his training in

medical science at a time of a revolution in medical education and, equally important, when bacteriology and experimental pathology were still relatively young disciplines. Each day, month, and year, bacteriologists and pathologists seemed to produce solutions or answers to age-old problems in medicine. The possibility of making a discovery endowed scientific research with an aura of hope, and it also proclaimed the ultimate usefulness of such activity; in so-doing, it gave further impetus to scientific investigation. Flexner was nurtured in this environment and, in time, contributed to it.

Another aspect to this time period should be stressed. The maturation of bacteriology and experimental pathology occurred almost simultaneously with the accumulation of capital by a vigorous, brawling, often ruthless generation of industrial and commercial entrepreneurs. When Flexner began his career, a good deal of that capital was already being channeled into a variety of philanthropic endeavors by an extraordinary troop of men who, for lack of a better term, might be characterized as a civil service of capital. It was, in part, the vision and activity of these men—among others, Frederick Gates, Wallace Buttrick, and Wycliffe Rose—which ultimately created institutions and programs that fostered scientific research. Philanthropy did not create scientists. It did help organize a social environment which permitted science and scientists to flourish. Put another way, one of the keys to the development of Simon Flexner's career lies in the history of the Baltimore and Ohio Railroad and the Standard Oil Company. In the end, The Rockefeller Institute for Medical Research, which Gates dreamed of and which Flexner breathed life into, created a frontier of science which had all of the phoenixlike qualities Turner thought had disappeared in 1890.

References

1. Turner, F. J. 1960. *The Frontier in American History*. New York: Holt, pp. 1–38.
2. Schlesinger, A. M. 1933. *The Rise of the City*. New York: Macmillan, pp. 157.
3. The early history of The Johns Hopkins Medical School is best recounted in Chesney, A. M., 1943, *The Johns Hopkins Hospital and The Johns Hopkins University School of Medicine, Vol. I, 1867–1893*. Baltimore, Maryland: Johns Hopkins University Press.
4. Flexner, S. *Manuscript Autobiography*. Chapter I, pp. 1–15. Discusses his early medical training. (Flexner Papers), Library of the American Philosophical Society, Philadelphia, Pa.

5. Dr. William T. Councilman (1854–1933); trained by H. Newell Martin in physiology at The Johns Hopkins University, was Dr. Welch's original assistant in pathology at The Johns Hopkins Medical School. In 1892, he succeeded Reginald Fitz as Shattuck Professor of Pathological Anatomy at the Harvard University Medical School.
6. Long, E. R. 1962. *A History of American Pathology.* Springfield, Illinois: Charles C Thomas, pp. 153–154; Flexner, S., *op. cit.,* Chapter IV (revised), pp. 43–44.
7. *Ibid.,* p. 44; Flexner, S., and Flexner, J. T. 1941. *William Henry Welch, and the Heroic Age of American Medicine,* New York: Viking, pp. 202–207.
8. *Ibid.,* pp. 50–51.
9. *Ibid.,* Chapter III, pp. 5–6.
10. Rous, P. 1949. "Simon Flexner 1863–1946." *Obituary Notices of Fellows of The Royal Society,* Vol. 6 (November), p. 413.
11. Flexner, S. *Op. cit.;* Chapter IV (revised), pp. 44–45.
12. Rous, P. *Op. cit.,* p. 413.
13. Flexner, S. *Op. cit.,* Chapter V, pp. 12–13.
14. *Ibid.* Chapter VI, pp. 1–3.
15. Flexner's early experiences at the University of Pennsylvania Medical School are best described in Flexner, S., *op. cit.,* Chapter VII, pp. 1–8.
16. *Ibid.,* pp. 8–10; *see also* Link, V. B., *A History of Plague in the United States of America,* 1955, Public Health Service Monograph No. 26. Washington, D.C.: Government Printing Office, pp. 3–8.
17. For Flexner's later experiences at the University of Pennsylvania, see Flexner, S., *op. cit.,* Chapter VII, pp. 10–19.
18. Corner, G. W. 1964. *A History of The Rockefeller Institute 1901–1953.* New York: Rockefeller Institute Press, pp. 1–30. See especially "The Recollections of Frederick Gates on the Origin of the Institute," Appendix I., pp. 575–584. Flexner, S., and Flexner, J. T., *op. cit.,* pp. 269–278.
19. Flexner, S. 1930. Report to the Members of the Corporation on "A Sketch of the First Twenty-Five Years of The Rockefeller Institute for Medical Research." Typescript, Oct. 31, 1930, p. 6.
20. *Ibid.,* p. 7.
21. Corner, G. W. *Op. cit.,* pp. 49–50.
22. Flexner, S. *Manuscript Autobiography,* Chapter VII, p. 4.
23. Shryock, R. H. 1947. *American Medical Research, Past and Present.* New York: Commonwealth Fund, pp. 39–73; Flexner, S., and Flexner, J. T., *op. cit.,* pp. 280–282.
24. Flexner, S. 1930. Report to the Members of the Corporation on "A Sketch of the First Twenty-Five Years of The Rockefeller Institute for Medical Research." Typescript (Oct. 31), pp. 15–16.
25. *Ibid.,* pp. 13–14.
26. Corner, G. W. *Op. cit.,* pp. 56–59.
27. *Ibid.,* pp. 77–80; 120–124; 167–170.
28. *Ibid.,* pp. 91–94; Benison, S. 1967, *Tom Rivers, Reflections on a Life In Medicine and Science,* Cambridge, Mass.: MIT Press, pp. 67–71.
29. Peabody, F., Draper, G., Dochez, A. R. 1912. *A Clinical Study of Acute Poliomyelitis.* Monograph of The Rockefeller Institute for Medical Research, New York, No. 4.
30. Benison, S. 1955. *The Reminiscences of Dr. A. R. Dochez, An Oral History*

Memoir. Typescript, Columbia University Oral History Research Office, p. 30.
31. *Ibid.*, pp. 32–34.
32. *Ibid.*, pp. 40.
33. *Ibid.*, pp. 41–42.
34. Benison, S. 1962. *The Reminiscences of Dr. Peter K. Olitsky, An Oral History Memoir.* Typescript (Author's possession). New York, pp. 10–12.
35. Corner, G. W. *Op. cit.*, pp. 144–148.
36. Flexner, S. 1920. Diary Notes, Dec. 6.
37. Benison, S. 1967. *Tom Rivers, Reflections on a Life in Medicine and Science.* Cambridge, Mass.: MIT Press, pp. 124–125.
38. Gasser, H. 1939. Report on the Activities and Problems of The Rockefeller Institute. Typescript, New York, October 3, pp. 19–20.
39. Dr. Flexner's development of an antiserum against cerebrospinal meningitis in 1907 was one of the factors central to the subsequent development of the Institute, in that it persuaded Dr. Gates of the utility of his idea of a medical research institute. See further, Corner, G. W., *op. cit.*, pp. 60–62.
40. Dr. Flexner's early successful research in poliomyelitis can be followed in Flexner, S., and Lewis, P. The transmission of acute poliomyelitis to monkeys, *JAMA,* 1909, 52:1639; The transmission of epidemic poliomyelitis to monkeys, A further note, *JAMA,* 1909, 53:1913; A report on experimental poliomyelitis, *Soc. Exp. Biol. Med.* 1909, 7:49. *See also* Benison, S., The Enigma of Poliomyelitis, 1910, *in* Levy, L. W. and Hyman, H. M. (Eds.), 1967, *Freedom and Reform, Essays in Honor of Henry Steele Commager,* New York: Harper and Row, pp. 232–254.
41. Flexner, S., and Lewis, P. 1910. Epidemic poliomyelitis in monkeys, A mode of spontaneous infection. *JAMA* 54:535.
42. Flexner, S., and Noguchi, H. 1913–1914. Demonstration of cultures of the virus of poliomyelitis. *Proc. New York Path. Soc.* 13:106; Experiments on the cultivation of the microorganism causing epidemic poliomyelitis. 1913. *J. Exp. Med.* 18:461.
43. William Keen to Simon Flexner, March 15, 1913 (Flexner Papers).
44. Robert Osgood to Simon Flexner, February 3, 1911 (Flexner Papers).
45. Simon Flexner to Robert Osgood, February 7, 1911 (Flexner Papers). Flexner's cooperation with other investigators can be followed in Benison, S. 1975. "Speculation and Experimentation in Early Poliomyelitis Research." *Clio Medica,* Vol. 10, No. 1, pp. 1–7.
46. The substance of Flexner's argument with Dr. Meltzer can be followed in Samuel Meltzer to Simon Flexner, July 23, 1916; Simon Flexner to Samuel Meltzer, July 29, 1916; Samuel Meltzer to Simon Flexner, July 31, 1916 (Flexner Papers). *See also* Samuel Meltzer, *Medical Record,* July 22, 1916, correspondence, pp. 159–160.
47. Simon Flexner to Helen Flexner, October 2, 1916 (Flexner Papers).
48. Benison, S. 1967. *Tom Rivers, Reflections on a Life in Medicine and Science.* Cambridge, Mass.: MIT Press, p. 111.
49. Sabin, A. B. 1940. The olfactory bulbs in human poliomyelitis. *Amer. J. Dis. Child* 60:1313; Benison, S., *Reminiscences of Dr. Albert Sabin, An Oral History Memoir* (in process), March 8, 1975, interview, p. 34.

II

OSWALD T. AVERY AND THE EVOLUTION OF MODERN BIOMEDICAL SCIENCE

A View of "Fess" in the Laboratory

MACLYN McCARTY

THE TITLE that was originally proposed for this talk was "A Young Scientist's View of 'Fess'." While I was undeniably at least relatively young at the time that I worked with Fess, I am very conscious of the fact that this was a long time ago. I am now older than Fess was when I came to his laboratory, and my image of him in those early years has been filtered through a long column of time, packed with other experiences. Thus, even though I believe that my recollections have not been modified substantially in the process, I opted for the more neutral title. The name "Fess," as I am sure most of you know, was short for Professor, and was widely used by his friends and colleagues. It was a nickname of warmth and affection that even found its way into his family. His young niece, for example, called him "Uncle Fess."

I came to the Avery laboratory in September, 1941, when it was in a period of transition. Colin MacLeod, after seven years in the laboratory, had left on July 1 to take the chair of microbiology at the New York University College of Medicine. At the same time, Frank Horsfall had returned to the fold as a Member of The Rockefeller Institute for Medical Research after his four years in the Virus Laboratories of the International Health Division of the Rockefeller Foundation. The plan appeared to be that Horsfall would be responsible for continuing a pneumonia study—presumably with emphasis on viral pneumonia—after the retirement of Avery, who was then in his sixty-fourth year.

The onset of the war late that fall, followed by plans to activate the Naval Research Unit at the Hospital, accelerated events so that Horsfall's separate laboratories for the study of viral pneumonia were soon in operation. Ed Curnen and Dick Mirick, who

had been engaged in the completion of projects initiated with Colin MacLeod, joined the Horsfall laboratory. Others nominally in the Avery laboratory in 1941 were Wally Goebel, who by that time worked independently on his own problems on the floor above, and Ernie Stillman, who did his own thing in his inimitable, eccentric fashion.

The point of this historical recital is to indicate that I was soon Avery's sole associate in the daily activity of the laboratory, and I found myself in an unusual one-to-one position with him. What a contrast to his laboratory in the twenties and thirties, when there was always a group of several young disciples working on various aspects of the pneumococcus! And what an opportunity for a young postdoctoral fellow!

Many of Avery's colleagues have commented on his methods of initiating a new member of his laboratory group: his refusal to assign problems; his insistence that the neophyte select his own, subtly guided, of course, by the indoctrination; and his well-polished monologues recounting in detail the paths followed by the various lines of past research, often referred to as Fess's "Red Seal Records." My personal experience with this process was a special one, partly because of the circumstances that I have just recounted. A second factor was the status of the problem of transformation of pneumococcal types. I have no doubt that Fess's burning desire to know the nature of the substance responsible for transformation before he retired from active work influenced the course of the process.

During the previous year, I had had a fellowship at New York University with William S. Tillett, a former student and close friend of Avery. Avery spent his summers near the Tilletts on Deer Isle, Maine, and he was a frequent visitor in their home, where I first met him in late 1940. (In passing, I should note that it was Tillett who was responsible for my opportunity to come to Avery's laboratory; he quickly made the necessary arrangements, when I was awarded a National Research Council Fellowship, with the stipulation that I broaden my experience by going elsewhere. Clearly, I was accepted by Avery on the strength of Tillett's recommendation.)

Being in New York, it was a simple matter for me to visit Fess in the spring and obtain from him a mass of recommended read-

ing material to peruse over the summer. Thus, by the time Fess returned from Maine in mid-September, I was prepared for my exposure to the Red Seal Records. These were not formally arranged discourses, nor were they offered as a systematic series. As often as not, they arose spontaneously during discussions in the laboratory, triggered by some point that had been raised or some question asked. They represented detailed accounts of the manner in which the several lines of research of the laboratory had developed—the rationale, the approaches, the reverses, the triumphs; in short, the real flavor of the investigation. They made fascinating listening the first, the second, and even the third time one heard them. They were certainly not memorized, but the logical order of the presentation and much of the phraseology had been carefully selected and were always the same. These discourses served not only to flesh out and reinforce the factual details that one had encountered in reading about the work, but also to give the research more reality and to touch on the human aspects that rarely appear in scientific papers. They probably also gave one the illusion of knowing more of the intimate details than was really the case.

This is how I first heard the full background on the story of the transformation of pneumococcal types and the nature of the continuing work on the phenomenon since the last publication on the subject from his laboratory seven years earlier. My interest in the subject must have been apparent to Fess, and one day he suggested that I get first-hand acquaintance with the phenomenon by setting up with him a test of the activity of the most recently prepared extract of the transforming substance. This is all it took. From then on, by common consent and without any formal decision having been made, I was engulfed in the problem. It was in this manner, then, that the matter of his assigning a problem and the necessity of my selecting one were neatly circumvented. He may have been pretty sure that I would be hooked once I started, but at least he did not have to deviate from his principles by suggesting directly that I work with him on transformation.

The simplicity of the laboratory in which these experiments were carried out was remarkable by today's standards. The space had been designed originally as a hospital ward—the ratio of clinical to laboratory space having been overestimated in plan-

ning the first research hospital in the country—and it had been converted for laboratory use with little modification. Desks with a microscope cabinet on one side of the kneehole and three drawers on the other were the basic units of laboratory furniture. Avery's personal laboratory was a small room that adjoined a larger, general laboratory area. It had apparently been a ward kitchen, and had swinging doors at each end fitted with small oval windows. It was not large enough to accommodate much more than the usual microscope desk, a refrigerator, and a cabinet for glassware and other supplies. The desk was placed against the single window, the dark shade of which was usually drawn. This formed a better background for reading precipitin and agglutination tests, and for inspecting tubes for evidence of the diffuse growth accompanying pneumococcal transformation, all with the illumination from a green-shaded, adjustable lamp hanging from the ceiling. This simplicity was matched by all of the laboratory rooms, none of which boasted equipment more complex than standard centrifuges. Sterile glassware—flasks, tubes, pipettes—were its stock in trade.

The image of Fess at work in his small laboratory recalls his meticulous technique in carrying out bacteriological procedures. This had its origins at the very outset of his career in bacteriology. When he began working at the Hoagland Laboratory in Brooklyn, he and his friend, Ben White, who directed the small laboratory, agreed that they would establish the routine principle of handling all bacterial cultures as though they were the plague bacillus. Thus, they sought to avoid that common frailty of relaxing standards of technique in dealing with bacteria that had little or no pathogenicity. Fess adhered to this principle of maximum care in handling bacteria, any bacteria, with great fidelity throughout his career. In addition to being eminently sound practice, it had the further virtue of almost eliminating the problem of contaminated cultures.

In practice, his technique involved a series of rituals that were rigorously followed in such things as unwrapping sterile pipettes, flaming the bacteriological loop, or manipulating the cotton plugs of sterile tubes and flasks. An experiment was not begun until the required tubes, pipettes, reagents, and racks were systematically arranged on the desk for ready accessibility,

and the Bunsen burner properly positioned. He would then draw the chair close to the desk so that the right hand, in which he held the pipette, could be stabilized by placing the right elbow firmly on the desk. The pipette, containing such material as sterile media or bacterial culture, would then be held nearly stationary, with the tip one or two inches from the flame of the Bunsen burner. The left hand would be used to move tubes and flasks to the scene of action, bringing them first to the fourth and fifth fingers of the right hand for removal of the cotton plug, then to the burner for flaming, to the pipette tip for delivery of the sample, back to the burner, and then to retrieve the plug. All this with almost no movement of the pipette. Miscues, such as touching the pipette to the outside of a tube or brushing a hand against an exposed cotton plug, resulted in immediate discard of the potentially contaminated material.

In many respects, his technique was bacteriologically conventional, but he had added several little touches of his own and carried out the procedures more meticulously and faithfully than is ordinarily the case. This almost compulsive concern with technical perfection in dealing with viable bacteria had an amusing effect on one aspect of the studies of the pneumococcal transforming substance.

In order to obtain enough material for the attempts to determine the nature of the transforming substance, it was necessary to grow pneumococci in rather large quantities. The organisms were grown in a clear liquid medium or broth made from an extract of beef heart plus added nutrients. After overnight incubation, a culture would contain roughly 500 million viable pneumococci per cubic centimeter—or, in terms more generally familiar to the layman, say more than two billion in a teaspoonful. They were not only viable but virulent, as indicated by the fact that a single organism would generally kill a mouse if injected appropriately.

These organisms, to which Avery devoted his career, have a diameter of 1/25,000th of an inch, which helps explain to the nonmicrobiologist how one can have two billion in a teaspoonful of culture.

Mass cultures for extraction of the transforming principle involved the use of 12- to 15-gallon lots of this broth, from which

the organisms had to be recovered by use of a special type of centrifuge. This consisted basically of a stainless-steel cylinder about 10 inches long and 1¾ inches in diameter which rotated in a vertical position at a high rate of speed as the fluid culture slowly passed through it, depositing the bacteria on the inner wall of the cylinder. At the completion of the process, one was left with some trillions of packed bacterial cells, which formed a solid mass with a consistency approximating that of a yeast cake, that somehow had to be removed from the rather narrow tube. This was done with an instrument consisting of a half-round, thin, metal plate machined to fit the inner surface of the cylinder and attached to a long metal rod. The bacterial cake was scooped out of the cylinder with this gadget and transferred to a beaker with the aid of spatulas. Residual material was washed over with salt solution that was also used to rinse the tools before sterilization.

It was Colin MacLeod, on one of his many visits to the laboratory during this early period, who guided my hand in my first experience with harvesting one of these large batches of pneumococci. I remember clearly that Fess left us alone while I was taught this basic procedure, and it seemed perfectly natural that he should do so. However, as I went through the process innumerable times on my own in the next few years, I gradually became aware that Fess *never* remained in the laboratory while the harvesting was in progress. If he happened to be present when the cylinder full of bacteria (carefully wrapped in lysol-soaked towels to take care of contamination of the outer surface) was brought up from the centrifuge room, he would quickly depart. While I could give no credence to the view, expressed by a technician in the laboratory, that this behavior was motivated by fear of possible infection, it took some time for me to realize what the answer was. It was simply that he could not bear to witness a procedure that deviated so far from his standards of correct bacteriological practice. He accepted its necessity for the research, but could not be a party to it.

It was indeed a messy operation. No matter how steady the hand that scooped the bacterial cake from the cylinder and transferred it to the beaker, there were bound to be little slips and sudden jerks. As a result, one would see small flecks of white

material fly in one direction or another with the disconcerting awareness that they were composed of millions of viable pneumococci. Despite all precautions and the liberal use of germicides, one could not complete the task without the conviction that he had thoroughly contaminated himself and the immediate environment. Small wonder, therefore, that Fess, with his early pledge to treat all bacteria as though they were plague, found it best to withdraw and pretend that his colleague was dealing with the problem in an acceptable fashion.

The first step, after mixing the bacterial paste with salt solution to form a creamy suspension, was to heat-kill the organisms. Although this was done to protect the transforming substance contained in the bacterial cells and not to protect the investigator, the technique converted it into a more manageable mess. Fess then joined with enthusiasm in the experiments involving extraction, purification, and testing of the transforming principle.

Our few years of working side by side on this fascinating biological problem were unquestionably exciting and stimulating. It was not all sweetness and light, however. There were many ups and downs, the surges of optimism followed by disappointment, and the inevitable set-backs. Fess, like all of us, was given to changes of mood, but during periods of dejection he dramatized his low spirits more overtly than one would have expected. This cast a damper on the spirit of the laboratory, and, in addition, these periods were associated with little spontaneous activity or conversation. Since he liked company in his inactivity, I was also involved, and I am afraid that I did not always bear with him as patiently as I might have. Nonetheless, the predominant and most enduring memories are of the good times: the exhilaration of the search; the encouragement of the interim triumphs, and the smell of success as the ultimate goal came into view. It was an extraordinary privilege to have shared these experiences with Fess and to have had the opportunity to learn from him during our years of intimate association. It has all been brought back most vividly in recent discussions with René Dubos in the course of his preparation of a much broader, more comprehensive picture of Avery's life. You will now be able to hear some of this directly from Dr. Dubos.

Fess Avery: The Man and the Scientist

RENÉ DUBOS

THE AVERY LEGEND was already well established when I first walked on these grounds in May, 1927. During the fourteen years that I worked in close association with Fess Avery—from 1927 to 1941—I had countless opportunities to observe the behavior patterns through which he came to be known as the most stimulating and most gracious person on this campus. He was truly an enchanting individual. I could elaborate on what Maclyn McCarty has told you of laboratory life in Avery's department, but instead I shall present other aspects of his personality that I discovered while preparing his biography. Old photographs, family documents, memories of his schoolmates, generate a picture of him somewhat different from the one formed during our associations with him. The adult person whom we knew becomes even more interesting and more appealing when we realize the extent to which his persona was a creation of his own making.

Fess Avery was born of British parents in 1877 in Halifax, Nova Scotia. His father, Joseph Francis Avery, was a Baptist minister, a mystical and flamboyant churchman. While still in England, Joseph heard a call from God to move to Canada and establish a Baptist church in Halifax, where he settled until 1887. That year he heard another call, this time to move to New York City, the city of sin. There he became pastor of Mariners' Temple, a missionary Baptist church at 1 Henry Street on the Lower East Side. This church is still standing, very much a center of community affairs as it was when Joseph Francis Avery was its pastor until he died in 1892.

Mariners' Temple was a poor church; it had no organ, and the

This paper was transcribed from the taped speech.

piano broke down shortly after the Averys' arrival. Fortunately, a young German member of the congregation was a good cornet player. Little Oswald and his older brother Ernest decided that they, too, could learn to play this instrument. By some obscure means, they acquired two old cornets and practiced with them on the roof of their apartment building. They soon became good enough musicians to play in the church and also on the church steps, from where they induced the wicked people of the Bowery to worship by their inspiring music. Indeed, Fess Avery became such a good cornet player that he received a scholarship from the Academy of Music in Brooklyn and once played in Dvořák's "New World Symphony" under Walter Damrosch. The cornet incident is of interest in revealing that, even so early in life, Avery was a determined person with much self-discipline.

In 1893, Avery entered Colgate Academy and in 1896 Colgate University, both located in Hamilton, New York. Colgate was then supported by the Baptist church, and it is probable that he was intended for the ministry, like his father. But this was not to be. His vigorous independence asserted itself at Colgate, with manifestations different from those of his early youth, different also from those of his adulthood.

He continued to play the cornet, but, more importantly, became the leader of the college band. One can get a fairly clear impression of the strength of his personality from pictures of him during the college years and from what his schoolmates wrote of him in the yearbooks. He was called "Babe," because he was small and slender, but his schoolmates thought him rather tough and conceited. This is the kind of thing they wrote about him: "Being a minister's son, he is blessed with a faith in Providence, second only to his faith in himself"; "He lives in New York City, except in the summer which he spends with the scions of America's saponaceous aristocracy." (Through the Baptist church, his mother, who was an enterprising person, had established connections with famous families—the Rockefellers, the Vanderbilts, the Sloanes—and the college yearbooks strongly suggest that Babe Avery was boastful of these social connections.)

His academic interests emerge clearly from the college records. He took no scientific courses, except the few elementary ones that

were compulsory. In contrast, he took as many courses as he could in public speaking, declamation, debate—anything that gave him a chance to perform in public. He was very good at it, as shown by the fact that he shared the honors in public speaking with his classmate Harry Emerson Fosdick, who was to become one of America's most celebrated preachers. As all the courses in the senior year were elective, Avery completely omitted the natural sciences that year, emphasizing instead philosophy and public speaking.

While at Colgate, he began to question the validity of the Christian faith. In his senior year, he and five other students asked one of the philosophy professors to organize for them a seminar to examine the basis of Christian teachings. Harry Emerson Fosdick, who was a member of the seminar, reports in his autobiography that Babe Avery one day stood on the steps of Alumni Hall and summarized the discussions with the statement: "Fellows, you know there really *is* a God." This extrovert behavior was compatible with the young Avery playing the cornet on the steps of Mariners' Temple, but appears surprising to us who knew him at a time, twenty years later, when he refused to make any public statement, not even when he could back it up with much laboratory evidence.

After graduation from Colgate in 1900, Avery entered the College of Physicians and Surgeons of Columbia University, and this despite his lack of scientific background. His grades were fairly good in medical school, except in pathology and bacteriology! While he frequently told stories of his Colgate years, he never mentioned his medical training. He obviously did not enjoy the experience, and in fact his classmates in medical school did not have a high opinion of his ability; they thought of him as one of those least likely to succeed because of immaturity.

Avery graduated from medical school in 1904 and joined a group practice in New York City for three years. On the rare occasions when he spoke of this period, he indicated that he was successful in his relations with his human patients, but was bored with their diseases. Fortunately, he soon found a way to escape from clinical work.

In 1906, the famous English bacteriologist, Sir Almroth Wright, delivered in New York City a series of lectures on phagocytosis

and on the measurement of the opsonic index. Avery attended these lectures, and was much interested in them. When the New York City Board of Health established funds for the study of opsonic indices in patients with respiratory diseases, he applied and was given a fellowship of $50 a month to that end. At about the same time, he also obtained a job with the Sheffield Dairy Company, also at a salary of $50 a month, to do bacterial counts on milk before and after pasteurization—a technique that had just been introduced here. His final commitment to a life of laboratory science came a few months later when by accident he met Dr. Benjamin White of the Hoagland Laboratory in Brooklyn.

Surprising as it may seem, the first American institution privately endowed for bacteriological research was the Hoagland Laboratory, which was established in Brooklyn in 1888, the very same year that the Pasteur Institute opened its doors in Paris. Cornelius Hoagland was a physician who had made a fortune by promoting baking soda and creating the Royal Baking Powder Company. It was because his grandchild had died of scarlet fever that he decided to create a medical research institute. The first director of the Hoagland Laboratory was Sternberg, of yellow fever fame, and Benjamin White was in charge of the bacteriological department.

Ben White had received a Ph.D. in organic chemistry from Yale and had later received additional training in bacteriology. When he met Avery in 1907, he was immediately impressed, and offered him a full-time job as his associate at $1,800 a year. Thus began a scientific collaboration that lasted until 1913. Avery and White carried out a broad series of investigations in many fields of bacteriology, ranging from the study of yogurt to that of syphilis. These investigations were not highly original, but were very competent. Their greatest importance was to give Avery a thorough preparation for his subsequent career. From the very beginning, he learned to master exquisite bacteriological techniques, as reported by McCarty. He also learned from Ben White to use chemical methods and chemical thinking in the study of bacteriological problems.

For example, he and Ben White extracted from tubercle bacilli a fraction having certain biological properties; they also studied the immunological characteristics of certain purified proteins. At

the Hoagland Laboratory, in other words, Avery took the habit of approaching bacteriological and immunological problems from a chemical point of view—an attitude that he maintained for the rest of his life. Whatever the problem, he would always ask: "What is the nature of the substance responsible for this or that phenomenon? What are the chemical mechanisms involved?" Such a chemical approach guided all his subsequent studies of pneumococcal infections and of the genetic transformation of pneumococcal types.

Dr. Rufus Cole, who was director of the Hospital of The Rockefeller Institute for Medical Research, had been impressed by a bacteriological study on tuberculosis patients that Avery had published in 1912. Cole invited Avery to join the Hospital staff as bacteriologist, to participate in the program on lobar pneumonia. Avery's role in this program was the typing of pneumococci and the preparation of therapeutic sera. That he was immediately effective in this work is obvious from the fact that, when Monograph No. 7 on Lobar Pneumonia was published by the Rockefeller Hospital in 1916, he was the senior author.

Avery was then almost 40 years old and still essentially unknown, except among a few of his colleagues. But the strength of his personality can be read in a document handwritten by him in 1916. It is a hospital record of a pneumococcus culture isolated from a pneumonia patient. The record shows a flamboyant handwriting that could hardly have been expected from a person reputed for his mild manners and shyness. I have collected more than 100 documents handwritten by Avery, and they show the same type of affirmative calligraphy to the end of his life, the sign of a man who knew what he wanted to do and liked to do it with a flourish, in a style all his own. I must mention in passing that this Hospital record is of great historical interest. The pneumococcus culture that it describes, D39, is one that was used extensively by all of us in the laboratory and that yielded the substrain used in the studies on genetic transformation of pneumococci and in the demonstration that DNA is the carrier of hereditary characteristics.

In 1917, Avery became an American citizen, was commissioned a captain in the U.S. Army, and had to conduct a

course on infectious diseases for medical officers. His lectures were so effective that the name Professor, later Fess, was attached to him for the second time. The first time had been when he was at the Hoagland Laboratory, when he lectured to nurses. One of his own stories illustrates the picturesque language with which he conveyed to his students the problems of contamination: "If your saliva were blue," he told them, "your patients would be living in a blue smog."

Avery began his scientific research at the Rockefeller Hospital in association with Dr. Alphonse R. Dochez, with whom he shared an apartment on 67th Street for the rest of his life in New York. They collaborated for only four years, but they continued to talk and dream science together even after Dochez left the Institute to join the department of medicine at Presbyterian Hospital. Whereas Avery had very little social life, Dochez went out almost every evening. But coming back from the theater or a dinner party, still in evening dress, he would sit on Avery's bed and tell him of the medical thoughts he had had while listening, for instance, to *La Traviata.* Time and time again, both Avery and Dochez stated how essential these late-night conversations had been in the development of their scientific concepts. There is no doubt, in any case, that the outcome of their collaboration was a series of important joint investigations.

These investigations were highly imaginative, but some of the conclusions were erroneous. At the risk of shocking Avery's admirers, I shall mention three of his published statements that were soon shown to be wrong. In 1916 and 1917, Dochez and Avery published in the *Journal of Experimental Medicine* a paper dealing with a phenomenon that they termed antiblastic immunity. In it, they claimed that the immunological mechanisms of resistance to pneumococcal infection are of only secondary importance; what happens first, they suggested, is that certain of the serum constituents inhibit the enzymes of pneumococci, and consequently their metabolic activity. According to Dochez and Avery, the immune antibodies came into play only after the antiblastic—antigrowth—processes had taken place. Within a very few years, their theory of antiblastic immunity was shown to be based on a misinterpretation of experimental findings.

Another erroneous claim was that the specific soluble

substances of pneumococci, which Dochez and Avery had discovered, were the toxins of pneumonia. This statement can be read in Monograph No. 7 on Lobar Pneumonia. Avery himself recognized a few years later that these specific soluble substances have, in fact, no toxicity whatever.

More surprising, and more relevant to the rest of my presentation, is that in 1917 Avery wrote in his annual report to the Board of Scientific Directors and published in the *Journal of Experimental Medicine* that the specific soluble substances of pneumococci are proteins. As is well known, he first achieved international fame six years later when he demonstrated with Heidelberger that they are not proteins, but polysaccharides. I suggest that, around 1920, Avery became aware of his propensity to make unwarranted scientific statements. He learned his lesson, and from then on became puritanical in his scientific language, acutely conscious of his duty never to go beyond established facts—in public, at least.

By 1920, also, there was clear evidence of two of the most striking aspects of Avery's genius, namely, his gift for recognizing an important biological problem, and his persistence in the chemical analysis of this problem. He recognized that, since certain soluble substances of pneumococci determine their immunological specificity, knowledge of the chemical nature of these substances would throw light on the mechanisms of biological specificity. He did not know enough organic chemistry to deal with these problems, and therefore tried to enlist the interest of the chemists whom he knew. One of them was Michael Heidelberger, who was then working in Van Slyke's department on the seventh floor of the Hospital, trying to crystallize oxyhemoglobin. Fess Avery carried in his pocket a small tube containing some of the specific soluble substance, and would shake it in front of Heidelberger, saying, "Michael, if we knew the chemical nature of this substance, we would understand the chemical basis of immunity and of biological specificity." Heidelberger tried to resist, but eventually yielded. And thus began their epoch-making collaboration.

Dr. Heidelberger has recently told me that, in fact, Fess Avery had gone very far by himself in the purification of the specific soluble substance, using his own methods of what he called

"kitchen chemistry." Within a very short time, in any case, Avery and Heidelberger made a fundamental discovery that was to change the course of immunological research—that the specificity of pneumococcal types is due not to proteins, but to polysaccharides located in the capsules of these organisms. From then on, Avery's department became the world leader in bacterial immunochemistry.

At first, there was much resistance to the view that polysaccharides were responsible for the immunological specificity of pneumococci. Most immunologists and chemists felt that polysaccharides could not have the chemical complexity required to account for biological specificity. They concluded that the preparations used by Heidelberger and Avery were contaminated with active proteins—a preview of the controversies that were to be stimulated twenty years later by Avery's statement that DNA is the carrier of hereditary characteristics.

Within a very few years, the immunological specificity of capsular polysaccharides was universally accepted, and Avery's department became fully engaged in various fields of immunochemistry. I shall mention only two items that illustrate the singleness of purpose and diversity of approach in the department at that time. Walther Goebel was working with Fess Avery on the synthesis and immunological study of artificial, synthetic antigens. Together, they synthesized an antigen containing a sugar selected because of its similarity to the sugars in capsular polysaccharides of pneumococci. With that synthetic antigen, they could immunize mice and render them resistant to certain types of pneumococcal infections; they could also produce sera effective in the treatment of experimental infections. That achievement remains to this day one of the most spectacular feats of immunochemistry.

Around 1930, Fess Avery and I discovered a bacterial enzyme that hydrolyzes the capsular polysaccharide of type III pneumococcus. Injection of the enzyme into mice, rabbits, or monkeys suffering from type III pneumococcal infection could rapidly cure these animals, thus proving beyond doubt Fess Avery's claim that the capsular polysaccharides are essential to virulence.

With much regret, I must now abandon this immunochemical phase of Avery's research program, and also overlook other research activities of the department, to focus my attention on the DNA phase of his scientific life.

Ever since 1917, Avery had been committed to the view that pneumococci were divided into several biological types, each of which had a distinct immunological identity. In 1928, however, Fred Griffith, a medical officer in the British Ministry of Health, published evidence that he could make pneumococci change type in the mouse. The claim was so shocking that our first reaction was to reject it as due to experimental error. Fess Avery, in particular, could not accept Griffith's findings.

There was in the laboratory at the time a Canadian physician and bacteriologist, Henry Dawson, who was part of the pneumonia clinical service. Dawson was bred of British culture, and he believed *a priori* that anything done in a British laboratory had to be right. On his own, he repeated Griffith's experiments and confirmed that pneumococci could indeed be made to change type in the mouse. Then he went one step beyond Griffith, and showed that the transformation of pneumococcal types could be brought about in the test tube.

In 1930, Dawson left the Rockefeller Hospital to take charge of the arthritis division at Presbyterian Hospital in New York. He was replaced on the pneumonia service by Lionel Alloway. By that time, Avery had accepted that pneumococci can undergo type transformation both in vivo and in vitro, and he urged Alloway to pursue the problem—or, rather, he played for him one of the Red Seal Records of which McCarty has spoken. It was Alloway who first demonstrated that pneumococci could be made to change type in vitro with a soluble material extracted from killed pneumococcal cells, and who obtained the first preparations of the viscous material that was identified as DNA a few years later by Avery, MacLeod, and McCarty.

Colin MacLeod replaced Alloway in 1935, and improved the techniques for the preparation of the transforming substance and for the determination of its activity. When he left in 1941, he was replaced by McCarty, who took the final steps in the purification of the transforming substance and identified it as deoxyribonucleic acid. The role of McCarty in this work was similar to the role

played by Heidelberger twenty years earlier in the chemical identification of the capsular polysaccharides. His chemical knowledge was greater than that of either Fess Avery or MacLeod, and he was thus able to bring the DNA work to completion. But Fess Avery provided the continuity, from the time he recognized the great significance of the problem through the many years of heart-breaking labor needed to elucidate its chemical determinism.

I shall now briefly review some other historical facts concerning the emergence of the DNA story and the public response to the classic paper by Avery, MacLeod, and McCarty in 1944, published in the *Journal of Experimental Medicine.* I shall also express my view of the reasons why this phenomenal achievement was not recognized by a Nobel Prize.

Some of our colleagues on this very campus have expressed the opinion that Avery did not appreciate fully the significance of the transformation phenomenon. If he had, according to them, he would have mobilized the resources of his department more effectively than he actually did for a more rapid isolation of the transforming substance and determination of its genetic effects. As they point out, many years elapsed between the first preparation of the soluble transforming material by Alloway and the publication in 1944 of the classic paper on DNA.

In reality, there were several independent reasons for the slow development of the work. First, it must be kept in mind that Avery's department was part of the Hospital, and that we were committed to the control of respiratory diseases, especially lobar pneumonia. This disease was then one of the greatest killers in the United States—some 50,000 people died of it every year. The mortality was of the order of 30 percent in certain types of pneumonia. We, as a department, were responsible for the care of pneumonia patients, the preparation of therapeutic sera, and the development of vaccines against the disease. The period was the 1930s, before the advent of sulfapyridine and of penicillin, at a time when the treatment of pneumonia was an extremely difficult medical problem. Dawson, Alloway, and MacLeod spent much of their time on the pneumonia ward, attending to heart-breaking clinical situations. Whatever our interest in other biological

problems, we could not forget our commitment to the control of pneumonia.

There were other difficulties from the research point of view. The transforming substance was extremely unstable. In fact, active preparations could not be stabilized until the time when McCarty recognized that the esterases of pneumococci depolymerize the transforming nucleic acids. Another difficulty came from the bacterial strain used to test the activity of the transforming preparations. Starting from the D39 culture, of which I spoke at the beginning of my presentation, much painstaking work had to be done before a strain was obtained with the proper "competence." Between 1935 and 1940, Colin MacLeod made remarkable contributions to the selection of a substrain of D39 that was suitable as a test organism. The work could proceed in a dependable manner only after these technical difficulties had been resolved.

As I discuss at length in the Avery biography, there was at first, and naturally, much skepticism concerning the claim that DNA was the substance responsible for the transformation phenomenon. More surprisingly, it was also claimed by certain groups that the 1944 paper by Avery, MacLeod, and McCarty had little, if any, scientific influence. For example, Gunther Stent wrote in *Scientific American* that the work of the Avery group had no significant impact on the evolution of modern genetics, because it could not be related to existing scientific knowledge of this field; it could not be fitted into "canonical knowledge." In reality, there is no ground for this assertion. Many biologists and chemists, young and old, immediately recognized the broad significance of the fact that hereditary transformation could be brought about by deoxyribonucleic acid. I have given many examples of this early recognition in the Avery biography, but shall mention only one here. In 1945, Avery was selected by the Royal Society of London for the Copley medal. The president of the Society was then Sir Henry Dale; in his citation he referred to DNA as the "gene in solution," and suggested that the discovery made it possible to study genetic phenomena by the methods of organic chemistry. There could not be a more explicit statement of the belief that the identification of the transforming substance had opened new approaches to the understanding of heredity.

There were, of course, legitimate doubts as to the chemical purity of the nucleic acid preparations that brought about the change of types in pneumococci, especially because it was believed at the time that nucleic acids did not have the structural complexity required to account for the diversity and the specificity of genetic processes. It was easy to imagine that the active preparations contained small amounts of unidentified materials—proteins, for example—that were responsible for the activity. In fact, Avery, MacLeod, and McCarty were acutely aware of this possibility. Avery, in particular, had constantly in mind the painful controversies which had followed the announcement, twenty years earlier, that proteins, and not polysaccharides, were responsible for the immunological specificity of pneumococci. The Avery group was so eager not to overstate its evidence that, in their historic 1944 paper, they acknowledged the possibility that some substance other than DNA was involved in the change of pneumococcal types.

The conservative and, indeed, almost pathologically cautious attitude that Avery had cultivated for more than two decades prevented him from receiving the recognition that he so richly deserved. The members of the Nobel Prize Committee recognized, of course, the potential significance of the discovery that transformation activity resided in DNA preparations, but they decided not to award the prize for this achievement until the findings had been more thoroughly validated. When Arne Tiselius was interviewed concerning the factors affecting the award of Nobel Prizes, he acknowledged that the failure to give it for the DNA work had been a mistake. He offered as an excuse that the 1944 paper was not sufficiently positive and that the Nobel Committee had decided to wait for further evidence. He also remarked that "Avery was an old man at the time of discovery," a surprising statement, since, although the Professor was then close to 65 years of age, he had retained all his intellectual vigor and eagerness.

After his official retirement in 1943, Fess Avery continued to work on transformation until 1948, first with Maclyn McCarty and then with Harriett Taylor and Rollin Hotchkiss. Finally, he decided that he was no longer capable of really contributing anything worthwhile to the work of his young colleagues, and he

left New York to join his brother in Nashville, Tennessee. There he engaged in some laboratory work at Vanderbilt University, but he especially lived as a country gentleman, deeply interested in the local flowers and participating in community affairs. Photographs of him at that period show a thoughtful, forceful person, but one at peace with the world. To the end of his life, he retained the marvellous control of himself that had enabled him to discipline his innate characteristics and to convert them into the most appealing and creative human traits.

As I remember Fess Avery, and as I think of what I have learned of him while writing his biography, I realize that there was a fundamental similarity in his scientific work and in the way he created his persona. In the last paragraphs of my book I tried to express in the following words that everything he did in his adult life had an artistic quality governed by self-discipline and a classical taste.

"He did not have a robust enough temperament to deal effectively with complex, ill-defined situations, such as those commonly presented by clinical and social problems, but he had immense intellectual vigor in selecting from the confusion of natural occurrences the few facts most significant for the problems he elected to investigate, and he had the creative impulse to compose these facts into meaningful and elegant structures. His scientific compositions had, indeed, much in common with artistic creations, which do not imitate actuality, but transcend it and illuminate reality.

"Avery applied disciplined creativeness both to his scientific work and to the development of his personality. He retained throughout his life the perceptive, intelligent, determined, and also impish and whimsical expression that had characterized him during his youth and college years. In adulthood and old age, however, his face radiated, in addition, tolerance, sympathy, wisdom, and a romantic inwardness. 'At 50, everyone has the face he deserves.' This was especially true of Avery, whose adult face achieved a rich mellowness that testified to the prodigious control he exerted over all aspects of his temperament. He certainly believed with Montaigne that each of us can 'discover in himself a pattern all his own' and that 'to compose our character is our duty.' In the end, his most glorious masterpiece was the

persona he created by cultivating at each phase of his intellectual and emotional development those aspects of his nature that made him function best in each particular situation.

"Those who have known The Professor admire him for what he composed as a scientist; but they remember him even more vividly for the art with which he composed his character and his life."

III

DETLEV W. BRONK AND THE TRANSITION FROM INSTITUTE TO UNIVERSITY

Herbert Gasser, Detlev Bronk

H. KEFFER HARTLINE

WHEN, IN THE SUMMER of 1923, I first went to Woods Hole to take the course in general physiology, I had the good fortune to have a letter of introduction to Jacques Loeb. I called on him in his laboratory in the small, wooden Rockefeller Building, across the street from Old Main. He was most gracious to a young student. He inquired about the work in the course (which he had initiated), and about my interests. I had brought with me the manuscript of my first research paper on phototropic responses of animals to light of low intensity. Loeb seemed genuinely pleased to find a student interested in tropisms. His own early interests had been in brain physiology, soon extending to tropisms and animal behavior. Although he was then working on the physical chemistry of proteins, these earlier interests were still bright for him. My paper was full of logarithms, histograms, standard errors, and the like—all in the spirit of "quantitative Biologie." After introducing me to Selig Hecht, to help me translate my college English into English, Loeb published my paper in the *Journal of General Physiology,* which he and Osterhout had founded a few years before.

Jacques Loeb's influence was profound in the whole of biology. Biology was to become a quantitative, rigorous science based on physics and chemistry. He was not the first, and not alone in this, of course, but he was one of the most effective leaders of his time.

Detlev Bronk, as a young graduate student of physics attracted to biology, was one of those greatly influenced by Jacques Loeb. He expresses the eagerness with which he read Loeb's book, *The Mechanistic Conception of Life.* Concepts he met with in that book, he writes, "led me across the ford between physics and

biology." Bronk had been urged to read Loeb's book by Simon Flexner, who also advised him to write of his interests to Osterhout, whom he subsequently met and who remained a lifelong friend. On reading Osterhout's monograph "Injury, Recovery and Death in Relation to Conductivity and Permeability," Bronk writes: "I, an embryo physicist, was lured to biology." The influences of Loeb and Osterhout must have been strongly felt in many of the diverse fields flourishing in this institution. Their insistence on quantitative experiments and their emphasis on physics and chemistry in biology were revolutionary for many fields at the time. Many of the changes here in the past two decades were made in the spirit they fostered, especially the addition of mathematics, physics, and, for Loeb particularly, the laboratories of behavioral sciences. The strong tradition here in my own field of neurophysiology, I believe, owes much to Loeb, with his interest in mechanisms of nervous function and in behavior, and also to Osterhout, whose basic studies of ionic permeability of cells lie at the foundations of modern work on mechanisms of nerve and synapse.

In the use of quantitative methods in biology, no one surpassed Herbert Gasser. Gasser owes his selection as Director of The Rockefeller Institute for Medical Research, we can be sure, to his well-recognized wisdom and broad scholarship, but also to his eminence in science. His scientific interests were wide-ranging; his special competence was in neurophysiology. Det Bronk came as close as anyone could to summarizing in a few words the scientific accomplishments of Gasser over years of meticulous work. Writes Bronk: "[Gasser] was enabled to define groups of nerve fibers, and relate them to specific sensory and motor functions. By measuring with great precision the magnitude and temporal courses of the action potential of nerve, he was enabled to classify the functions of the groups of fibers comprising nerves and to follow the progression of basic cellular processes."

I remember seeing, on a visit to St. Louis, the early, if not quite the original, equipment used by Gasser, Erlanger, and Bishop in those truly revolutionary studies: the electronic amplifier, built of quaint devices called vacuum tubes, and the cathode ray tube—Braun tube—on the end of which originally only the faint fluorescence of the glass had revealed the form of the compound

nerve action potentials. The first photographs, I was told, were made by pressing a piece of film against the outside of the glass. Some of you may have seen the up-to-date equipment in Gasser's laboratory in Theobald Smith Hall that he used during his vigorous retirement. It was the highly evolved descendant of that early apparatus.

Gasser attracted many able associates, and when he came here he established a laboratory that was one of the leading centers of neurophysiological study. Of Gasser's associates, I knew best two: Rafael Lorente de Nó and David Lloyd. They are outstanding scientists, leaders in their fields. They are both retired from The Rockefeller University, active elsewhere; but to those of us who know them well, they are still with us in our respect and regard.

I cannot claim to have been a close friend of Herbert Gasser, but our friendship was warm. Occasionally, I enjoyed hospitality at his apartment. He was a warm, witty, and gracious host, with cultural depth and breadth that I could only envy with admiration.

But Det Bronk and Herbert Gasser were indeed close friends. Colleagues in science, they traveled to meetings together, they visited often, they chatted, they argued, they joked. They owned a house jointly in Woods Hole. Herbert liked sailing, but it was by no means the passion with him that it was with Det. I am not sure that Herbert and Det ever sailed together. Could it be that Herbert actually believed those tales that Det and I told of our sailing experiences?

Gasser and Bronk, brilliant scientists, masters of an exacting specialty, both broadly versed in many other fields, were deeply concerned about the educational needs of young scientists just starting their careers. They must have had many discussions of educational philosophy and of the future of the Institute during their many years of close friendship—Herbert the Director, Det a member of the Board of Scientific Directors.

Most of you are familiar with Det Bronk's career. With his newly acquired degree in both physics and physiology, he went to England to work with A. V. Hill in London and with Adrian in Cambridge. Adrian and he developed the methods for recording the action potentials of single nerve fibers, thereby pioneering

the "unitary analysis" of nervous function. When, subsequently, he was appointed Director of the Johnson Foundation at the University of Pennsylvania, Det and his co-workers applied this analysis to the study of the nervous regulation of the circulation—work that has become classic.

Det was a vigorous and enthusiastic laboratory worker. It was inspiring to work across that hall from his lively laboratory, through many busy and productive days—nights, to be more accurate. To his associates, he was a stimulating colleague and a sincere friend. And the informal hospitality he and Helen lavished on us all enriched our lives. That Bronk tradition was enjoyed on this campus by many of us who are here today.

The improvement of graduate education was one of Det Bronk's foremost concerns. He remembered his own graduate school experience. He was influenced by the writings of Loeb and Osterhout, as I have mentioned, and by his associations with Hill and Adrian. He had learned that the study of biology in terms of physics and chemistry required freedom and flexibility for students to choose their own course of training; he understood their need to start that training early. A graduate university came into his thinking.

At the Johnson Foundation, his ideas on graduate education developed and matured as he had opportunity to put some of them into practice. Det's scientific renown attracted to his laboratory able postdoctoral fellows. But it was not long before he arranged to have predoctoral graduate students, as well. They were free to take whatever courses in the University of Pennsylvania they needed, but they spent most of their time in the laboratory in research. They soon became competent colleagues. A number of them have reached eminence.

Much of Bronk's thinking on graduate education and much of his inspiration came from Gilman's concept of a graduate university at Johns Hopkins. When Det left the Johnson Foundation to become President of Johns Hopkins, before he came here, he hoped to advance toward Gilman's goal, which had become his own. Part of the Gilman vision was realized. Barriers between undergraduate and graduate study were reduced, so that able students could move as fast as their ability permitted to advanced study, no longer tightly constrained by the formal lock-

step of traditional academic progression. This "Hopkins Plan" has been a continuing success at Johns Hopkins.

Upon Detlev Bronk's appointment as President of The Rockefeller Institute for Medical Research, when Herbert Gasser retired, the Institute's course broadened as it transformed itself into The Rockefeller University. As you shall hear, it was to establish additional fields of study and research; it was to build on its great strength as a renowned research institute, in a city rich in opportunities for broad cultural experience; it was to encompass graduate education based on the research that students and faculty would pursue together as colleagues, but with the flexibility and freedom, thoughtfully guided, that a beginning student should have. With steadfast cooperation of trustees, faculty, and, by no means least, the incoming students themselves, Detlev Bronk's goal was reached as he led in our continuing experiment in American education.

Detlev Bronk and the Development of the Graduate Education Program

FRANK BRINK, JR.

WE ARE CELEBRATING the seventy-fifth anniversary of this institution, which is devoted to the advancement of science through research and the education of young scientists. For the last twenty-two of these seventy-five years, this institution has been a graduate university, admitting students who are candidates for academic degrees. I have been invited to describe the transition of The Rockefeller Institute for Medical Research into The Rockefeller University—an evolutionary process started in 1953 by two actions of our Board of Trustees. In that year they decided to incorporate the Institute, under the Board of Regents of the State of New York, as a graduate university, empowered to grant the degrees of Doctor of Philosophy and Doctor of Medical Science, and they appointed Detlev W. Bronk to be the new president. I will tell this tale with frequent quotations from speeches, letters, and annual reports of the president. In this way, I hope to avoid too much retrospective interpretation of events and policies.

The Idea

The Rockefeller University, as a graduate school of science, was an idea in Det's mind long before it materialized through the coordinated efforts of the Board of Trustees, the faculty, and the students. Det thought that the proper task for a professional scientist is creative synthesis of available knowledge for the special purpose of designing experiments likely to yield new knowledge. He believed that synthesis of scientific knowledge leads to new philosophical insights benefiting mankind intellectually, culturally, and morally. For him, the ideal scientist is

a scholar who utilizes scientific criteria in ordering and re-ordering our collective knowledge of the natural world. Such a person, he thought, must be inquisitive, imaginative, logical, and, above all, sincere—a knower and a doer with, it is hoped, a great capacity for communicating his knowledge to others. Therefore, Det's conception of the ideal graduate university of science was an environment that would foster the development of such latent traits in young scientists, and would make advanced study and research an exciting adventure for each student. There were two groups of people required for this purpose—a faculty with such scholarly traits, and students with a strong motivation to learn science for the special purpose of personal participation in research. At the first academic convocation, Det expressed such ideas formally:

"Since the beginning of The Rockefeller Institute, only a half century ago, it has provided rich opportunities for men to learn. It has been a community of scholars who were privileged to explore the frontiers of natural knowledge. Our predecessors have left us a heritage of traditions of intellectual excellence and adventure. They laid strong foundations for a house of learning. . . .

"Five years ago we determined to build further on those foundations, so that we might welcome our young successors to this community of scholars and gladly teach and guide them as they prepare for scholarly careers."

The persons composing a graduate school are traditionally divided into three groups: faculty, postdoctoral fellows, and graduate students. The scientific staff of The Rockefeller Institute for Medical Research included the first two groups and, in 1955, a few graduate students were appointed. Initially, this was the bare fact of transition from research institute to university. The original charter provided for education and research, including provision for postdoctoral fellowships and the related apprenticeship training in experimental research. The only revision of the original charter that was required in 1953 was the legal right to grant specified academic degrees.

However, the appointment of graduate students in 1955 must have seemed an abrupt change to those members of the faculty who had come to the Institute before 1953. I surmise this because

in the Descriptive Pamphlets from 1937 to 1954 one can read:

"The departments of the Institute are organized for research only. Under normal conditions no provision is made for the enrollment of individuals or classes for formal instruction in the medical sciences or in laboratory or clinical methods. Thus, the Institute absolves its staff from the necessity of devoting time and energy to formal teaching or to the consideration of subjects and problems chosen for reasons other than because of their value and promise for the advancement of science."

Clearly, in 1954, some changes were imminent. A new interpretation of the final phrase "value and promise for the advancement of science" had been created during the preceding two years by Det Bronk and a committee of the Board of Trustees, who were charged with the task of projecting the second fifty years for the Institute.

Graduate Fellows

In that same year, we established our new laboratory for biophysics in Theodore Smith Hall, just above Herbert Gasser's laboratory. Det had an office there, as did I. It was during this period that he asked me to give some serious attention to specific academic aspects of his plans for graduate education in the Institute. It was clear that there were exceptionally competent scientists on the faculty with wide-ranging professional interests in medical sciences, biology, biochemistry, biophysics, neurophysiology, and physical chemistry. He planned to appoint a number of visiting professors concerned with other disciplines. The immediate problem was how to select exceptional students to match an exceptionally able faculty. In his annual report for 1955–56, Det described to the Board of Trustees how this was done.

"We have proceeded on the theory that those who have been intimately associated with a student's undergraduate education are best able to judge his aptitude for graduate study and a career in science. Accordingly, I described our educational ideals and program to the presidents of a score of colleges of liberal arts in whom I have high confidence and to the chairmen of departments of science in a dozen large universities. To each of these

we entrusted the appointment of a 1955 graduate of his college or university to an Institute fellowship.

"From Amherst, Dartmouth, Haverford, Oslo, Pennsylvania, Smith, Union, Wesleyan, and Yale came the first ten students who were selected."

Then, and later, Det spoke often of the necessity for selecting the students with the same care as used in selecting members of the faculty. Therefore, he said, we should accept only those students whose commitment to advanced study and research matched that of our faculty. He knew that the kind of graduate university that would emerge depended critically upon selecting dedicated and competent students of science. For the next twelve years he personally interviewed most of the prospective students invited to the campus by our admissions committee.

Advanced Study and Research

During this early period, Bronk worked directly on all aspects of the academic program. He was assisted by a Faculty Committee for Educational Policies: Alfred E. Mirsky, René Dubos, Lyman Craig, Alex Bearn, and Edward Tatum. The general academic policies of the Institute had already been described in his letters soliciting appointees and in his appointment letters to students. They were formalized in his statements in the Descriptive Pamphlet for 1956. Therein he wrote:

"The students are considered to be intellectually mature and are assumed to be capable of self-directed study. Accordingly, there is little formal instruction; teaching is mostly done in seminars, tutorial conferences, and in faculty research laboratories. Students have little opportunity to be passive recipients of formal teaching; they have much freedom for the active process of learning."

However, we were not sure that we would find enough college students who could begin their graduate studies in this ideal manner. Therefore, a later paragraph in the same pamphlet states:

"The educational program is designed to suit the needs and interests of the individual student. The orientation seminars reveal the need and prepare the way for more specialized study. Because most students have been required to learn through

formal lectures and prescribed reading in secondary school and college, two types of educational opportunity are available during the early stages of graduate education at the Institute. For those who desire a gradual transition to more independence, there are formal courses such as cytology, biochemistry, and physiology which comprise lectures, seminars, and laboratory work. Those who are ready for greater freedom are encouraged to develop their own programs of study and research; the faculty are then available as advisers and leaders of seminars rather than formal teachers."

These paragraphs stated our intentions, but when they were conceived there were no organized courses here. My assignment was to develop an academic structure in which the student could effectively engage in advanced study of science while immersed in an atmosphere of intense commitment to research.

The long experience of the faculty with postdoctoral training made them superior advisers for graduate students undertaking research for a thesis. Therefore, our main concern was the creation of opportunities for advanced study in the form of courses and seminars. We evolved an idea that was later made explicit in the "Guide for Graduate Students." The academic structure of the University was to be based upon the proposition that in graduate education there is no significant separation of advanced study and research, that is, of learning from the recorded experiences of other scientists and learning from direct observation of natural phenomena. The graduate fellows were to study the logical structure and content of organized scientific knowledge for the special purpose of effectively planning pathways to new knowledge.

Thus, technical skills would be acquired by apprenticeship in the research laboratories. The opportunities for learning were to include self-directed study of advanced textbooks and of professional journals, tutorial instruction in special topics, and seminars for sharing information and for learning to communicate professionally with experienced scientists. There was no core curriculum, and each student designed his own program of study, with the aid of his faculty committee. There were as many curricula as there were students!

Some of our initial concern about how to involve an exclusively

research-oriented faculty in academic matters was unfounded. A significant number expressed their interest, and the students, in seeking research advisers, automatically involved others. Thus, twenty-six of the faculty lectured in the Seminars on Contemporary Science during 1955–56. In January, 1956, the first authentic course, biochemistry, was organized by a faculty committee appointed by the president. Bill Stein delivered the first lecture in this first formal course on January 30, 1956. The topic was "Purity of Proteins." During the next four months, thirty-nine members of the faculty lectured or conducted laboratory sessions, reflecting the intense concentration of biochemical talent in the research laboratories at that time. About half of those lecturers are still here on our tenured faculty or among our emeriti.

This was an auspicious beginning to the development of several formal courses, each reflecting the scientific interests of a rather large number of the faculty. Det and I were elated when Keith Porter and George Palade offered to give a course in cytology, starting in February, 1957. The third course, physical chemistry, was organized by Theodore Shedlovsky for 1958.

Within three years after the arrival of the first students, formal courses were enticing as many participants as were tutorials and seminars. The increase in the number of courses reflected, in part, the opinion of some faculty members that coherent subjects are best taught formally, rather than by self-directed study and consultation with the faculty. Moreover, courses in basic subjects were deemed necessary because many competent students wanted and needed further formal instruction in mathematics, physics, biochemistry, physical chemistry, organic chemistry, and cell biology. The response of the faculty to requests from the students was beginning to be a major factor in determining the development of an academic structure within the research institute.

What academic policies have survived the test of experience with more than four hundred graduate students and a more diversified and larger faculty, each member with his own ideas about the proper environment for advanced study and research? To indicate the continuity of academic style and purpose, I have selected some sentences from the 1961 "Guide for Graduate

Students" that can be found (with improved wording) in various parts of the "Guide" for 1975—fourteen years later.

"At the Rockefeller University emphasis is placed on the development of the individuality of the potentially creative scholar. The objective of the faculty is to provide an environment in which a student can develop scholarly abilities in accordance with his personal interests and motivations. The varied creative potentialities in a group of young scholars should become manifest during a period of graduate study. Assessment of such achievement in terms of comparison with an average for a group is meaningless, and is avoided. In this University a sufficient condition for steady progress of a student is a compatible association with an able research adviser. Such an adviser not only guides the student toward technical competence but makes maximal effective use of all of the faculty to ensure that his advisee becomes not merely well-trained but also well-educated."

Clearly, the present academic policies reflect the continuing influence of Det Bronk's concept of an ideal university of science as a "community of scholars" in which the younger members are tutored by older and more experienced scientists.

Continuity and Change

In 1954, too, there were discussions of the intellectual scope of an ideal graduate university of science. Our breadth in biological sciences was to be extended to the behavioral sciences and complemented by more faculty members concerned with physics, chemistry, and mathematics. Eventually, a faculty in philosophy and history of science was deemed essential. The new faculty members were to be selected for their excellence in creative scholarly work, attracting to the University superior graduate students and postdoctoral fellows. We expected that the wider range of intellectual activity of the faculty would expand the scholarly efforts of the students. We hoped that the diversity of interests among such a small group of students would promote, spontaneously, a broader range of advanced study by each one, complementing the narrower specialized training so necessary for a professional career in research.

Although it is definite that the transition to university status began by a vote of the Board of Trustees in 1953, the completion of the transition is less evident. Of course, the first convocation in 1959 was an exciting milestone of progress. The University had its first alumni—five of them! However, the expansion of the faculty was just beginning. In a report to the Board of Trustees in 1961, Det announced the appointment of Ludwig Edelstein as professor by stating:

"It is only of incidental significance that he is a distinguished historian of biology and medicine. It is of deep significance that he is a great humanist; as a community of scientists we have suffered too long from lack of association with scholars such as he who is versed in the origins of modern science and the influence of science on the ideas and habits of man."

In 1954, there were biologists, biochemists, biophysicists, and physical chemists engaged in research here. By 1964, there were also physicists, mathematicians, and a humanist among our professors. And by 1974, with professors of logic and philosophy added, the faculty seemed well-rounded, if not complete. Thus, the evolution of the faculty seems continuous when sampled every ten years. We can look forward with great interest to the next sampling point in 1984.

For many years, the range of scientific research has exceeded that generally expected of an "institute for medical research." In the Descriptive Pamphlet for 1937 one can read:

"The scope of the Institute's work is wider than the study of problems whose solution has an immediate application to human pathology. It has, in fact, been the principle of the Institute's organization that it can best serve medical science by devoting a great deal of attention to the investigation of fundamental biological, physical, and chemical subjects. These aspects of science, as well as those of direct clinical importance, have been constantly under investigation, and, together with problems of general biological interest, have largely occupied certain of the scientific staff and have used a considerable share of the Institute's budget."

Det Bronk believed, too, that a synthesis of biological and

physical sciences was essential for future progress in understanding living systems. In 1956 he wrote:

"The purpose of the Institute is to further natural science; there is an especial emphasis on the life sciences and their application for improvement of human welfare. . . .

"Those who carry out these activities are a faculty of nearly two hundred, representing many fields of biology, medicine, and the related physical sciences." He continues with: "One of the distinguishing characteristics of The Rockefeller Institute is the flexible and personal nature of its organization; it is built around individuals rather than departments. This provides freedom for faculty and students to study and do research in any field of science they choose without regard for the inhibiting restrictions of departmental barriers. The helpful association of workers on diverse, related problems is encouraged. The synthesis of science is thus fostered."

This research policy remains explicit now, for in 1974 Fred Seitz wrote in his Report of the President:

". . . this University has not swerved from the conviction that it should concentrate on the life sciences and the related behavioral sciences. Nevertheless, our institution would not be a true university of sciences without mathematics, and physics programs of the highest quality. We should not lose sight of the contributions made to basic scientific knowledge and to our University by our mathematicians and our experimental and theoretical physicists. Their presence reinforces the spirit of intellectual adventure and the rigorous standards that pervade our community of scientific research. They help to reduce the formidable barriers of disciplinary language that inhibit communication between those working at the outermost limits of physics and biology today, and they enhance the opportunities for interdisciplinary ventures involving both faculty and students."

Resumé

Thus, the Institute entered into and has progressed half-way through its second half-century with a continuity of style and purpose in research coupled to a creative change in the scope of

its educational efforts devoted to the "advancement of science." It is a unique graduate university, providing an environment of intense scientific investigation in which truly exceptional students can develop a strong commitment to professional research and a deep interest in the philosophical, logical, and historical foundations of natural science.

IV

DEDICATION OF THE DETLEV W. BRONK LABORATORY BUILDING

Dedication of the Detlev W. Bronk Laboratory Building

PATRICK E. HAGGERTY

IT IS A SOURCE of profound regret that on this day of shared memories and celebration of the University's 75 fruitful years, Detlev Bronk's voice will not be heard. It leaves a shadow on an occasion at which we had expected to enjoy the personal recollections of the pilot of the transition from Institute to graduate university of the sciences. But in his absence, we still can do him honor.

Out of all the photographs or portraits I've seen of Detlev Bronk, two seem particularly appropriate. One, reproduced in the University's 75th anniversary album, shows him striding briskly across a corner of the campus, matching—stride for stride—and conversing animatedly with a much younger colleague.

The other is the portrait in South Laboratory showing him in the full glow of his maturity as scientist, educator, and statesman, smiling and looking confidently out at the campus and associates he loved so well.

Immensely gifted and deeply involved in many worlds, one of Dr. Bronk's finest traits was his interest in others—he reached out to many in all walks of life and inspired them to achieve.

Closely related to this concern was his keen awareness of the importance of the environment in stimulating the human spirit and inspiring great works. We need only look around on this June day to appreciate how—under his enthusiastic leadership—this campus became a harmonious blend of old and new, of leaf and stone, of natural beauty and physical resources extraordinarily well suited for learning and research.

It is most appropriate, then, that today and in the presence of Mrs. Bronk, we should dedicate one of the buildings constructed

during his years as president to the memory of Detlev W. Bronk. South Laboratory with its many facilities and varied equipment for research and teaching is a fitting choice.

It is indeed an honor for me, as chairman of The Rockefeller University's Board of Trustees, to announce the renaming of South Laboratory as Detlev W. Bronk Laboratory—a physical symbol of his lifelong service to science and society and a concrete expression of gratitude for his inspiring leadership here at Rockefeller.

V

THE UNIVERSITY: CLIMATE OF EXCELLENCE

The University: Climate of Excellence

DAVID ROCKEFELLER

On March 8, before an international audience here in Caspary Auditorium, I expressed my concern about a growing tendency in our society to subordinate the idea of excellence to social and economic demands identified with the principle of equality. By excellence, I mean simply the pursuit of the best a human being or an institution is capable of in any realm of endeavor—the peaks toward which we all strive in our work and in our contribution to the sum of things. Excellence implies the highest standards of achievement against which individuals and societies can and should measure themselves.

The conflict between encouraging excellence on the one hand and promoting greater equality for men and women on the other is as old as our nation. Both goals are, of course, not only appealing but, in fact, imperative. It seems to me, however, that hard and misleading lines have been drawn in recent years which have placed the two goals in a position of unnecessary confrontation. In fact, there are disturbing signs of a fundamental breach between the growing thrust for equality and the traditional respect for excellence.

Where once it was sufficient, if not always easy, to work toward equality of opportunity and equality before the law, the newly emerging standards ask us to reach for absolute equality. And where there is conflict between excellence and this kind of egalitarianism—as there often is in such fields as education and scientific inquiry, or in the assignment of a democracy's most challenging tasks to the best-suited and best-equipped—excellence is too often required to give way. I surely need not remind this audience of the problems created for institutions like ours by fears on the part of some that the processes of advance-

ment and recognition based on merit seem to threaten a more rigid contemporary interpretation of egalitarian values.

This afternoon, within the University family, as it were, I should like to focus more narrowly on these concerns and explore the subject of excellence in the context of the University's founding and its subsequent seventy-five years. It is a history familiar to us all, but I think there are still insights to be gained from viewing it as an experimental model of how excellence is fostered and achieved. I say "experimental" because a spirit of adventure, an eagerness to be surprised and guided by experience, has always characterized this project known first as The Rockefeller Institute for Medical Research and now as The Rockefeller University.

Now that all those path-breaking articles from the scientific journals and all those finely crafted instruments from the shops are on display, it seems almost inevitable that, once founded, the Institute and then the University should have produced great things. Yet the *New York Times* reminds us, in a recent editorial, that before that founding, biological and medical investigation in this country "was essentially a cottage industry dependent on the accidents of genius and circumstance. . . ."

In effect, my grandfather and those who played the key roles in organizing the Institute proposed a course which could have been interpreted as a solution to this problem. They created an institution designed to foster research excellence systematically by bringing together the most qualified scientists that could be found and providing them with ideal conditions in which to work. The emphasis, from the start, was on people—outstanding people who could be expected to do great things. To laymen like Frederick Gates and my grandfather, the distinction between pure and applied science could not have been as clear as later developments—and much debate—have made it. But the remarkable staff that was recruited for the fledgling Institute was made up almost entirely of individuals who, by inclination and training, saw the need for basic knowledge and preferred to pursue it rather than to take the more superficially appealing course of aiming directly at practical results.

This course and this process did not represent arrogant elitism. The new institution began its operations quite modestly and

without flourish of trumpets. In fact, I believe my grandfather was fully prepared for the possibility that the Institute might pass from the scene after serving as a model for others to follow. Gates himself predicted that such an institute "would result in other institutes of a similar kind . . . until research in this country would be conducted on a great scale. . . ."

The results outstripped the promise, as we know. Under Simon Flexner, the institution was given a distinctive style and a powerful direction. Himself a pathologist and bacteriologist, he stressed the application of biochemistry and the physical sciences to research in the life sciences, an approach that still underlies the investigations in progress at the University. The instrument exhibit in the Caspary Gallery enables us to see some of the ingenious artifacts inspired by that approach. The list of early research achievements, particularly in the study of infectious diseases, is a catalogue of excellence. But above all, the Institute attracted scientists from all over the world, many at the start of distinguished careers, who found their inspiration in the experimental freedom and the high standards which characterized the Institute.

Under the directorship of Herbert S. Gasser, who succeeded Dr. Flexner in 1935, there was a broadening of the research program to intensify exploration of life processes on the cellular level, and, for the first time, the Institute undertook studies of the structure and function of the nervous system. Spanning as it did the latter years of a major depression and a world war, Gasser's tenure was troubled by economic and social pressures that threatened to jeopardize the institution's basic standards and scientific productivity. But the challenge was successfully met, and when I succeeded my father as chairman of the Board of Trustees 26 years ago, all the prophecies of Gates had come true. The Institute's influence had permeated science both at home and abroad. Scores of research centers—many of them founded and staffed largely by scientists trained at The Rockefeller—had been set up around the country. In fact, as he had forecast, the Institute was no longer unique. The concept of research exemplified by the Institute had proved to be justified, and other sources of support for this concept had materialized to create other institutions that were doing its kind of work.

It is significant that this situation was greeted not as an excuse for elation, but as a spur to reappraisal. If the goal had been reached, how, then, could we justify the Institute's continued existence and the expenditure of additional millions? Could the endowment now be applied more fruitfully to other needs?

These were questions that were raised as the decade of the fifties began, and by 1953, when Dr. Gasser retired, they were seriously troubling me and my fellow trustees. As you know, a committee headed by Dr. Detlev Bronk was formed by the trustees to review and evaluate the Institute's activities. The reappraisal—the first major one since the Institute's founding more than fifty years before—was thoroughgoing and forthright. Some of the prestigious scientists who were consulted argued that the institution should be liquidated and its funds redistributed among the nation's medical schools. Detlev Bronk, speaking for the committee, dissented eloquently and vigorously. The trustees as a whole weighed his arguments and agreed. Most of you here today are, by virtue of your own careers, bearing witness to the soundness of the decision to continue in the manner in which the Institute's mission was redefined. The time had come to put still greater stress on what was from the beginning a real concern of the Institute—preparing people for scientific scholarship and leadership. Hence, the change from the Institute to one of the world's few exclusively graduate universities was not a sudden revolution, but rather a reaffirmation and an expansion of prior objectives, a reaching out to new opportunities for the pursuit of excellence. Or, as Det Bronk phrased it: ". . . the legitimation of what had always been there in spirit."

Significantly, in announcing its recommendation that our institution should be continued and strengthened, the committee stressed the need to continue the institution's independence in human and material resources, and reaffirmed its policy of nondepartmentalization. The committee also confirmed that "the present policy of freedom from all programmatic, or project research should be continued."

I think it will take a long time for us to appreciate fully the extent of Det Bronk's contributions to this University. Some of them have already been summarized for you today by his closest

former colleagues. What I should like to stress particularly in my remarks is his extraordinary gift for picking and inspiring good people at every stage of their scientific careers. Under his leadership, we continued to attract and to train the brightest minds, who quickly took their places in other research institutions which were also expanding in those "go-go years" of the fifties and early sixties. And when, in his enthusiasm to make this a true graduate university of the sciences, he expanded the fields of research, he was able to fill the new posts with the best investigators from each field.

Under Det Bronk, the University proved it could handle its expanded role with distinction. The transition was a great adventure.

By the late 1960s, however, the climate for science was changing, and challenges to traditional concepts of excellence were mounting. These, coupled with financial pressures compounded by inflation and an energy crisis, made it obvious that the University would have to face up to another reappraisal. Under these changing conditions, the University could not possibly hope to sustain the rate of growth set in the previous decade and a half. Inevitably, there had to be a readjustment, a stabilization that would slow the pace without eroding the University's unquestioned position of excellence.

That readjustment was begun under the leadership of Fred Seitz, and is still in progress. It continues to be severely complicated by financial and social pressures. Can we continue to support excellent scientists and give them the independence and the climate to do their best work?

The answer is, "We must and we will."

No matter what the constraints upon us, we shall continue to do important things with distinction. But this can be accomplished only if we continue to support and encourage excellence in research and education. There are pressures in many universities and laboratories to water down standards. We here at The Rockefeller University must never allow that to happen.

Regrettably, there will have to be austerities for the moment, and we will require new independent resources for the future. Despite this University's great financial strength, if we are to sustain its special character over the next few generations we must

obtain additional endowment and operating funds. As Dr. Seitz has outlined in recent annual reports, we plan no further expansion in the near future. Yet we plan to regain a measure of dynamism by shoring up our independence, so central to our flexibility and excellence in research. Over-all, we shall maintain roughly the present level of research with some natural adjustments as special opportunities present themselves.

In recent years, as you are aware, federal grants to the University have increased continuously in an ever-more competitive market. That we could attract these grants is a source of pride, but any greater reliance on such funding foreshadows increasingly negative effects. For the best solution to the University's financial problems, we must rely on private initiative. Our future—and that of other leading private institutions in this country—depends on the degree to which we can achieve a broader base of private support from persons, foundations, and corporations with the resources and foresight to invest in excellence.

As for myself, I am just as strongly committed to working personally to help the University through this transition as I was when elected chairman 26 years ago. Though I turned that responsibility over to Patrick Haggerty last fall, I have, as you know, continued on the Board of Trustees and, as Chairman of the Executive Committee, I am actively involved in assessing all of our choices and in personally obtaining support for the University. I have enlisted, if you will, for the duration.

Fortunately, at this critical juncture in our country, I think that The Rockefeller University is recapturing some of the unique qualities it had when it was founded. Many institutions that achieved greatness so quickly in the affluent fifties and early sixties are now afflicted by an entirely new set of strains, strains they are not as well prepared to cope with as we are. Building excellence is a long process and demands constant vigilance. If suddenly this University and its Hospital are once again perceived to be more relevant to the mainstream of human needs, it is primarily because they had been sticking all along to proven values at a time when "relevancy," more than excellence, was the catchword for every passing fancy.

The pursuit of relevancy, it seems to me, was beset by a confu-

sion of values not unlike that which underlies current attempts to extol justice and fair dealing in human affairs at the expense of excellent achievement and the intellectual and material support it merits. If the price of achieving equality in its most complete sense is the degrading of excellence, then the American experiment will have failed in two short centuries. Certainly one of the basic faiths of our democracy is that excellence and all the values associated with meaningful equality must exist together.

What can be done?

Even looking back on the limited experience of a single institution like this over a short span of seventy-five years, it is plain to see what benefits for all men can come from the nurture of excellence. It follows that the members of this audience share a dual responsibility—to uphold the need for excellence in our society and to continue to strive to bring its fruits into everyone's life.

I think that the events I have just reviewed demonstrate that the responsibility can be shouldered without arrogance and with full concern for the worth and dignity of every individual. As one review said recently of a book by the physicist Victor Weiskopf, his writing shows concern for "the complementarity of compassion and curiosity in relation to the human condition." It is in this spirit that we must approach the task of demonstrating and defending the need for excellence in a society of free men and women.

VI

THE ROCKEFELLER UNIVERSITY: COMMITMENT AND CHANGE

The Rockefeller University: Commitment and Change

FREDERICK SEITZ

On behalf of the entire University community, I would like to thank all of the participants in our program today. Mr. Flexner and Professors Benison, McCarty, and Dubos have recalled the splendid abilities of Dr. Flexner and Dr. Avery, two of the extraordinary leaders of the Institute in its first half-century of unparalleled accomplishments. Professors Hartline and Brink have captured the spirit of Det Bronk's equally remarkable contributions to the transformation of our campus while he continued to insist on the highest standards of excellence. Those crucial standards have been nurtured by David Rockefeller at our institution for nearly four decades, and we are proud of his confidence and sustained participation in our mission.

In a moment I shall outline a few thoughts about the process of commitment and change at the University, but first I must note that it is not possible for me to chart a master plan. We try to administer the University's affairs with care, so that a strong future will be assured. But the most exciting frontiers in the future will be pushed back in unpredictable ways by the many talented people who serve here every day; and we will be aided by many friends, advisers, and collaborators throughout the world.

We are convinced that two general lines of actions are essential to preserve our institutional integrity and dynamism in the long run. With respect to public service, we are trying to broaden the understanding of the University's uniquely productive program, and to enlarge our base of private funding so that we can strengthen the core of independence and flexibility. With respect to internal concerns, we are dedicated primarily to sustaining the highest standards for quality in the few tenured appointments we make each year and in the younger scientists we select for our

prized programs of predoctoral and postdoctoral training. I might add that, unlike many other institutions, we have a relatively uniform age distribution at the tenured level, so that we may offer continuing hope to some of the oncoming generation of scientists who would like to join our permanent staff. Of course, we also must control our financial resources closely, aiming to eliminate the burden of our operating deficit before the end of this decade.

These two broad objectives—enlarging public understanding and support, and insuring internal standards and coherence—are being pursued with continuing consultation about our choices. As we succeed in these efforts, I believe we will be able to stabilize our strengths and to seize new opportunities in research serving society.

The past seventy-five years have brought enormous changes both to our society and to the matters that interest the creative scientist. Such changes obviously could not leave our institution unaffected. Before going on to discuss some of these changes, I think we should underscore, not without pride, that we have remained steadfast to most of the basic precepts we inherited from the University's founders. They include:

> the pursuit of quality, with the suppression of routine;
>
> an involvement in long-term research at the clinical level on the diseases of man, while conducting basic research in relevant areas of the natural sciences;
>
> preservation of the autonomy of the senior scientists in the selection of their fields of research, while encouraging interlaboratory cooperation;
>
> and a deep commitment to education, complementing a primary commitment to research.

As David Rockefeller has just reminded us, these are the things that, taken together, define the style of this institution.

It is true that we have lost some of our previous independence through the need to seek outside funds, rather than relying entirely upon endowment. Yet this process has opened our doors to many members of the greater society in which we live who have a profound interest in our work and well-being and have,

thereby, enriched our associations. Similarly, we have increased our cares, as well as our rewards, by the addition of a successful graduate school which involves some of the routines normally associated with formal education. But our largest educational activity continues to be at the postdoctoral level, where we have about twice as many colleagues as we do at the predoctoral level.

The areas of most significant, and indeed continuing, change on our campus over the years relate to the active fields on the moving frontier of research. It is true that we still retain a profound interest in the infectious diseases, both bacterial and viral, which were our main areas of interest until the age of antibiotics. But there is now a strong shift of interest toward the metabolic diseases, such as those involved in arteriosclerosis; toward cellular pathology, as in aging and cancer; and toward genetic diseases, such as sickle cell anemia. Associated with all of these is a growing awareness of the influence of environmental factors upon the various forms of disease—factors ranging from the incidental by-products of civilization to the countless pharmaceutical agents now being dispensed so widely.

Along with these changes in clinical interests, parallel changes are taking place in basic research as new opportunities and understanding occur. Some of the choices of areas of basic research, such as those related to cancer, are stimulated by widespread concern about special diseases. But most grow out of revelations on the frontier of science as we seek enlightenment concerning countless aspects of the organic and inorganic world, and gain new capabilities and insights relating to the composition and structure of molecules, to cell constituents and surfaces, and to the behavior of large aggregates of cells, including entire organisms.

There was a time between 1950 and 1970 when it appeared to some individuals that basic knowledge at the biomolecular level, such as that related to the structure of DNA, was unfolding at such a rapid rate that our interest in clinical research could profitably be downgraded or dropped. We know now, perhaps with the vision of hindsight, that this acceleration in the discovery of basic knowledge, to which we are contributing, places more, rather than less, responsibility upon us to give renewed emphasis to clinical research. Such research, however, must be

in keeping with the long-range traditions we have evolved at our University, whereby the ultimate sources of a given disease are tracked down with unremitting dedication and with the use of all of the tools made possible by the advances of basic science. Indeed, as the work of Avery, McCarty, and MacLeod demonstrated so clearly, this pursuit often provides new scientific insights of the most basic kind.

About ten years ago, while still a resident of Washington, I attended a meeting of our Board of Trustees to which Dr. James Shannon had been invited in order to discuss his views on the future of our institution. He was just in the process of leaving the directorship of the National Institutes of Health, after nearly twenty dynamic years in which he had been able to remold that organization in a most remarkable way, basing his concepts in part on the successes of our own institution. We flew back to Washington together and, during the journey, he expressed doubt that it would make much sense to continue our research hospital in view of the changing patterns of research within medical schools—made possible, for the most part, through federal funds. Several years later, Shannon was a member of our own faculty. Witnessing the ways in which the Washington legislators were now modifying his well-planned organization and its program, he altered his opinion, and agreed that our clinical program would continue to be an almost unique national asset and deserved a very high priority of attention.

What of the future of this University? I need not dwell here for long on the financial hazards faced by all private institutions in these days when double-digit inflation looms as a threat to solvency and independence. Our success in acquiring federal funds, when combined with the warm responses we have received so far in our quest for private gifts and grants, indicates that, as long as we adhere to our traditional role as an institution devoted to the natural sciences, with a major interest in the fields of biology, including biomedical research, we will fare as well as any other private institution. I deeply regret that so much of the valuable time of our scientists must be devoted to grantsmanship. However, that seems to be an unavoidable preoccupation for most members of the scientific community in our time. Perhaps one day our nation will develop better ways of support-

ing its creative scientific genius, but one cannot be optimistic about the short-run prospects.

It seems clear that the science of cell biology, which is fundamental to modern medicine, is entering a new phase as we move out from the very solid base provided by the innovations of Albert Claude, Keith Porter, George Palade, and Christian de Duve, and gain further understanding of such matters as the role of the cell surface and the factors which determine cell differentiation. While it would be an overstatement to say that the central activity of our institution in the future will be the further exploration and clarification of cell biology at the molecular and macroscopic levels through the use of all the tools and concepts science can provide, that work must clearly remain one of our major interests in the foreseeable future.

Similarly, we have an abiding involvement in the field of immunology, in which so many new developments are occurring at both the macroscopic and the molecular level. As the work of Henry Kunkel in connection with the autoimmune diseases and that of Gerald Edelman on the molecular aspects of the immune system demonstrate, such research continues to open up vast new vistas on the mechanisms of intercellular communication and response and adds to the practical knowledge of medicine, as well as to basic science.

We have had a strong commitment to the field of neurophysiology ever since Herbert Gasser became our leader. This base was broadened and strengthened during Detlev Bronk's period with the addition of a number of laboratories, including those devoted to physiological aspects of psychology, animal behavior, and child learning. We shall, at some point in the future, enter into a period in which the ground-work will have been laid for an attempt to understand the working of the brain—one of the most challenging of all the problems of biology and one which will bring together the disciplines of neurophysiology, cell biology, biochemistry, and communications theory into what will undoubtedly prove to be a most remarkable concert.

Probably the only other problem in the field of the life sciences which offers a comparable challenge is that centering on the origin of life on earth. It is difficult for me, at least, to believe that

anything resembling the final word has been said on this topic, although there is now good reason to believe that amino acids existed or were generated in the primordial waters of the primitive earth. The great gap which separates our present conceptions of the state of matter on the surface of the primitive earth, with its essentially inorganic composition, and the delicately complex structure of a living cell of our time, displayed in Keith Porter's remarkable pictures, is simply much too vast to be passed off without scientific concern of the first magnitude. Closing that gap of understanding must remain a major objective of the basic biological sciences.

To return to the issue of understanding the functioning of the brain, one may grant that there probably is a physical-chemical basis for understanding its routine operation as a device which receives, stores, processes, and reads out information. One may wonder, however, if the finer sensitivities of the mind that we associate with the terms consciousness and subconscious, and with realization of self—as well as countless other nuances which guide our actions and mean so much to us as part of the process of being alive—will find a ready explanation in terms of the cold facts of biochemistry, cell organization, and communications theory. Will we instead, even when armed with the basic knowledge of the functioning brain derived from present approaches, still be far from comprehending what the poet would call the real issues of life?

The field that is now termed physics was the first of the areas of natural science to intrigue the philosophers as, in the historical evolution of science, they attempted to put the universe in order. In fact, Aristotle was the first individual to attempt to write a textbook of physics. Buridan, Galileo, Kepler, Descartes, and Newton walked in his footsteps, illuminating the road much more clearly and broadly, but speaking a similar language. The science of physics stayed very close to its speculative philosophical origins during much of its initial phases, probably in the main as a consequence of the fact that the awakening scientific mind was deeply awed by the overpowering concept that the world is subject to universal natural law.

However, some of the members of the physics community, particularly those in the English schools, became overconfident

of their powers of analysis and conceptualization in the decades after Newton, and had the temerity to move several steps ahead and envision the universe in terms of a huge, mechanical, deterministic clock-work structure which had been wound up and made to run in accordance with the prescriptions of Newtonian law. That was the heyday of the notion of the luminiferous ether and the mechanical theory of action at a distance.

This classical structure came apart and to a crashing end early in the present century, when it became necessary to grapple with completely new formulations of such concepts as simultaneity, mass, space-time, quantized energy states, the duality of particles and waves, and the uncertainty relations. This experience has brought the more contemplative physicists back much closer to their philosophical roots, as indeed Ernst Mach suggested would be the case long before the turn of the century.

Even today, fifty years after discovery of the Heisenberg-Schroedinger formulation of classical quantum mechanics, the physicist stands in awe of the principle embodied in that formulation which requires that the human observer and his measuring equipment be taken into account in interpreting the atomic laws.

If there is a basic weakness in the state of development of the life sciences at the present time, I believe it is associated with the almost universal, overconfident acceptance of a mechanistic conceptual framework, analogous to that exhibited by classical physics in the last century. I grant that it may be the proper outlook for our time, because we are, with the use of tools both old and new, erecting a magnificent and useful edifice in a brilliantly heroic attempt to understand what is one of the most remarkable and awesome phenomena in the segment of the universe that lies within our ken, namely life. In pursuing the present course, we shall undoubtedly uncover many facts concerning the properties of living systems that are both enlightening and beneficial. All this is well and good.

However, while pushing ahead with all the speed our resources and imagination permit, we must preserve—along with our élan—an element of cautious modesty and humility in relation to the subject we pursue. For it may well happen that issues will arise in the systematic study of living systems that

will be far more subtle and revolutionary than our present conceptual framework, with its deterministic notions of a chemical clock-work, would suggest. Somewhere along the road ahead, the biologist may find comfort in consorting with the physicist on a far more intimate scale than might seem conceivable to most of us in the room at the present time.

BIOGRAPHIES

Biographies

SAUL BENISON is professor of history at the University of Cincinnati and also professor of environmental health at that university's medical school. He has served on the faculties of the College of The City of New York, Sarah Lawrence College, Long Island, Brandeis, and Columbia universities. While at Columbia, he was a key figure in the Oral History Research Office, and has since been an adviser on oral history to many organizations. He has compiled more than a score of oral history memoirs on leading figures in varied fields, including Peter Olitsky and Thomas Rivers of The Rockefeller Institute for Medical Research. His book *Tom Rivers: Reflections on a Life in Medicine and Science* is considered a model for the organization and use of oral history materials. Dr. Benison is currently at work on a history of poliomyelitis and The National Foundation. He also has a deep knowledge of Simon Flexner's career, a subject he hopes to write a book about in the years ahead.

FRANK BRINK, JR., professor at The Rockefeller University, has been closely associated with its education and research programs. In 1958, Dr. Brink was appointed to the newly created post of Dean of Graduate Studies, a position in which he served until 1972. As a scientist, he has been engaged in research on the biophysics and biochemistry of excitable cells. Before joining The Rockefeller Institute for Medical Research as a Member in 1953, Dr. Brink had taught at Cornell University Medical College, the University of Pennsylvania, and The Johns Hopkins University. He served from 1953 to 1959 on the Divisional Committee for the Biological and Medical Sciences of the National Science Foundation. From 1962 to 1965, he was one of twelve educators and scientists named by President Kennedy to membership on the Presidential Committee for the National Medal of Science, and chaired the committee for two years. Dr. Brink is a member of the National Academy of Sciences and the American Academy of Arts and Sciences.

RENÉ J. DUBOS, professor emeritus at The Rockefeller University, is a microbiologist and experimental pathologist who first demonstrated—more than 40 years ago—that germ-fighting drugs can be extracted from microbes. Among his other scientific achievements are the development of a rapid method for growing tubercle bacilli in sub-

merged cultures, important in the study of tuberculosis, and investigations on the mechanisms of acquired immunity, natural susceptibility, and resistance to infection. He is also an award-winning author, whose lectures and books have alerted an international audience to the effects that the total environment exerts on all forms of life, and have placed Dr. Dubos in the forefront of ecological studies. His most recent book is *The Professor, the Institute, and DNA,* a biography of the late Oswald T. Avery of the Institute staff with whom Dr. Dubos worked closely, just published by The Rockefeller University Press.

JAMES THOMAS FLEXNER is the son of Simon Flexner, the first director of The Rockefeller Institute for Medical Research, and is a historian with broad interests. One of his first books, *William Henry Welch and the Heroic Age of American Medicine,* he wrote in collaboration with his father. This was followed by *Doctors on Horseback: Pioneers of American Medicine* and several other books dealing with medicine, American art and civilization. He was awarded the Parkman prize in 1962 for *That Wider Image: The Painting of America's Native School from Thomas Cole to Winslow Homer.* More recently, his four-volume biography of George Washington, which has rescued the first president from contradictions and caricatures, won for the author a National Book Award and a special Pulitzer Prize citation. Mr. Flexner is also a contributor to magazines and newspapers, and is a popular lecturer.

PATRICK E. HAGGERTY became chairman of the Board of Trustees of The Rockefeller University in 1975. He had been a member of the Board since 1970. Mr. Haggerty received the B.S.E.E. degree from Marquette University. In 1945, after serving for three and one-half years in the U.S. Naval Reserve during World War II, he joined Geophysical Services, Inc., in Dallas, Texas, where he was responsible for the development of research, engineering, and manufacturing phases of the company's operations. When Geophysical Services evolved into Texas Instruments, Mr. Haggerty became, successively, executive vice president and director, president, and, in 1966, chairman of the Board of Directors, retiring in April, 1976. He continues serving as a general director of Texas Instruments. He is the recipient of honorary degrees from a number of universities, and has long been active in affairs of science, particularly where they intersect with public policy. He has served on many civic and other associations, was chairman of the National Council on Educational Research, and a member of the President's Science Advisory Committee.

HALDAN KEFFER HARTLINE, professor emeritus at The Rockefeller University, is a world-renowned biophysicist whose pioneering

studies on the electrophysiology of the retina have exerted a major influence on the entire field of vision research and related areas. In 1953, Dr. Hartline joined the staff of The Rockefeller Institute for Medical Research as professor and Member. Immediately prior to his appointment, he was professor of biophysics and chairman, Jenkins Department of Biophysics, at The Johns Hopkins University. He had also been an associate professor of physiology at the Cornell University Medical College and professor at the Eldridge Reeves Johnson Foundation for Medical Physics at the University of Pennsylvania. In 1967, Dr. Hartline was awarded the Nobel Prize in physiology or medicine, shared with George Wald and Ragnar Granit. In 1972, he was named to the Detlev W. Bronk Professorship, the first endowed chair established at The Rockefeller University. He held this post until 1974, when he became professor emeritus.

MACLYN McCARTY has been associated with The Rockefeller Institute for Medical Research and The Rockefeller University since 1941. He has been a professor, physician-in-chief of the Hospital, and, since 1965, a vice president of the University. He has been highly influential in the development of clinical investigation in the Hospital and supervised the clinical research facilities at the University. He collaborated with the late Oswald T. Avery and the late Colin MacLeod in the classic experiments which, in 1943, led to the demonstration that deoxyribonucleic acid (DNA) is the substance in chromosomes that transmits hereditary information. Dr. McCarty has received many honors for his scientific contributions to various areas of research, including the transformation of pneumococcal types, the biology and immunochemistry of streptococci, and rheumatic fever.

DAVID ROCKEFELLER succeeded his father as chairman of the Board of Trustees of The Rockefeller Institute for Medical Research in 1950. In that capacity, he led in the conversion of Institute to University, retiring as board chairman in 1975, when he became chairman of the executive committee. Six years after receiving the Ph.D. degree in economics from the University of Chicago, Mr. Rockefeller joined the Chase National Bank, and when it merged with the Bank of the Manhattan Company, Mr. Rockefeller was appointed executive vice president in charge of development. In 1969, he became chairman of the Board of Directors and chief executive officer of The Chase Manhattan Bank, N.A., and of The Chase Manhattan Corporation. Mr. Rockefeller has received honorary doctor of laws degrees from several universities, and in 1975 was awarded the Legion d'Honneur in the Grade of Commander by the president of France. He is active in numerous educational, cultural, philanthropic, economic development, and investment enterprises,

particularly those which promote understanding and cooperation with foreign countries.

FREDERICK SEITZ, who has been president of The Rockefeller University since July, 1968, began his career as a physicist specializing in the theory of solids and nuclear physics. Before coming to The Rockefeller, Dr. Seitz had been president of the National Academy of Sciences for seven years. Previously, he had served as professor of physics, department chairman, and dean and vice president for research at the University of Illinois. Dr. Seitz serves as a member of or consultant to many national and international committees, including the White House Advisory Group on Anticipated Advances in Science and Technology. He is chairman of the board of the John Simon Guggenheim Foundation and a trustee of the University Corporation for Atmospheric Research. He has received more than twenty honorary degrees from universities here and abroad, and in 1973 was awarded the National Medal of Science.