

HOW MY LIGHT IS SPENT

The Memoirs of Dewitt Stetten, Jr.

Spring 1983

ON HIS BLINDNESS

When I consider how my light is spent
Ere half my days in this dark world and
wide,
And that one talent which is death to hide
Lodged with me useless, though my soul
more bent
To serve therewith my Maker, and present
My true account, lest He returning chide,
"Doth God exact day-labor, light denied?"
I fondly ask. But Patience, to prevent
That murmur, soon replies, "God doth not
need
Either man's work or his own gifts. Who
best
Bear his mild yoke, they serve him best.
His state
Is kingly: thousands at his bidding speed,
And post o'er land and ocean without rest;
They also serve who only stand and wait."

Sonnet XVI
John Milton
1608-1674

P R E F A C E

Apologia

These are the recollections of a blind man. Not that I was always blind. I have worn spectacles since four years of age to correct a severe familial myopia. The correction was good and the myopia had the advantage of giving me microscopic vision when I took my glasses off and held an object about two inches from my face. Undoubtedly, my chronic dependence upon having spectacles contributed to my distaste for games such as baseball and tennis and to my insecurity in such activities as swimming. It was in the late 1960s, while residing in New Brunswick, New Jersey, that I first noted the visual anomaly that led fairly promptly to the diagnosis of macular degeneration. I have since been seen by a number of ophthalmologists who have accepted this as the principal diagnosis with various supplemental diagnoses including bilateral cataracts and possible "soft glaucoma." The latter diagnosis, which implies a transient and occasional increase in intraocular pressure, might explain the fact that, in addition to the loss of central vision, I also exhibit very considerable reduction in peripheral vision.

About 1978 I found that I could no longer read, which was upsetting since reading had been a very important part of my life. I therefore asked to be relieved of my onerous duties as Deputy Director for Science, NIH, and about a year later I became Senior Scientific Advisor and moved to my present office at Stone House. Since then I have filled my life with tapes, records, conversation, seminars, and frustration. It was during this period that my oldest daughter, Gail, suggested to me that I write down some of my adventures and experiences. It was, of course, a figure of speech. Blind men cannot readily write. However, I could still dictate, a craft which I had practiced for many years. I therefore undertook the job and soon found myself engrossed.

It was only later that I recognized that what I was doing was fulfilling the therapeutic regimen prescribed by the late Adolph Meyer. This renowned psychiatrist, long director of the Phipps Clinic of the Johns Hopkins Medical School, often instructed his patients to set down their life histories on paper. This proved to be useful psychotherapy. And so, indeed, it has been in my case. After completing the first chapter I sent it off to Perspectives in Biology and

Medicine, a journal with which I have been associated since its founding, and was gratified to see it accepted for publication. I consulted with the editor, Richard Landau, about the possibility of publishing other chapters, and it was on his advice that I subsequently sought to have the assembled volume published.

When I had finished the first draft of this book, I noted that there was very little in it about my immediate family. In one of Mark Twain's novels he notes in the preface that there is no weather in the text. He therefore provides a wide choice of weathers in the preface and invites the reader to insert them at appropriate places. In analogous fashion I shall introduce here the several members of my family.

Gail was our first-born, raised in Bethesda and Woods Hole, educated at Douglass College of Rutgers, The State University of New Jersey, with a Ph.D. in yeast genetics from the Department of Biology of Brown University, and a postdoctoral experience in human cytogenetics at the Children's Hospital of Harvard Medical School. She is married to Peter Maloney, whom she met while in graduate school. He is a physiologist with particular interest in mechanisms of transport across cell membranes. He received an opportunity to join the Department of Physiology at the Johns Hopkins Medical School and, subsequently, Gail found work there as director of the cytogenetics diagnostic laboratory of the Department of Obstetrics and Gynecology. Here she is responsible for the workup of amniotic fluids secured from women in early pregnancy, whose babies are at risk for Down's syndrome or other genetic defects.

She is the mother of two delightful children --Beth, born in 1973, and Alex, born in 1976. Since they live within one hour's drive of our house, we see them quite frequently and our relations with our grandchildren are intimate and gratifying. Gail, who as a small child was always somewhat compulsive, has mellowed as a result of a prolonged illness from which, happily, she has now recovered, and has developed into a warm and sensitive young woman.

My second daughter is Nancy, one and one-half years younger than Gail. She was always our political radical. She selected the University of Chicago, where she spent about 10 years completing both baccalaureate and Ph.D. degrees. Her field of specialty was political science--and more specifically, Russian studies. Nancy learns languages with relative ease and has mastered Russian both as a written and a spoken language. While a graduate student she met and married Frank Einstein, who was earning his Ph.D. in English

Literature. After failing to find suitable teaching opportunities in Chicago, Frank and Nancy moved to West Virginia where he found a position at Davis and Elkins, a small church-related college. Their first baby, Joseph, born in 1977, has a round face and bright red hair resembling my own in infancy. A few years ago Nancy and her family pulled up roots to accept positions at Fisk College in Nashville, Tennessee. This is a black school with many problems. But then Nancy and Frank always liked problems. He is teaching English and she political science. Within the past few years their second child, Anna, arrived.

My third daughter, Mary, entered the Oberlin Conservatory to study voice. She soon decided, however, that the concert stage was not for her so she transferred to the academic program. Upon graduation from Oberlin she selected teaching of small children as her career area, and to prepare for this she secured a master's degree from the Bank Street College in New York. It was while teaching at an elementary school associated with the United Nations that she discovered that very small children could be introduced to science provided the right language and the right experiments were selected. This novel approach developed ultimately in her publishing a book, Let's Play Science, which described many of the exercises that her kindergarten students enjoyed. The book was hand lettered and illustrated by Mary, who has a peculiar talent for drawing mice and rabbits. In this volume the experiments were performed by mice and rabbits, not upon them. Since that time, Mary and I have collaborated on a couple of thin volumes in which I have composed doggerel which she has supplemented with illustrations. So far these books have not been published. Mary has taught science to first- through sixth-grade students at the Walden School in New York City and is married to Michael Carson. Mike is a theatrical producer specializing in industrial shows, which are generally one-night stands in exotic resort areas where the staff of one or another affluent company gathers to be recharged. He has, of course, aspirations to produce serious drama on or off Broadway and will doubtless get there someday. In 1982 this marriage was blessed by the birth of Matthew, a delightful baby with a particularly ready grin.

George is our youngest. At a very early age he exhibited interest in both science and music and we started him with piano lessons when he was very young. While resisting parental pressure to practice, he always had great facility in playing by ear and in improvising. Furthermore, he has had a

talent in hitting the "objective" examinations which have now captured the field of education. Although he did not impress his teachers at Rutgers Preparatory School from which he graduated, he was accepted at Harvard College where he spent four years making friends, amateur music, and adequate though not brilliant grades. He graduated in the field of applied physics, which is Harvard's equivalent to engineering, and then surprised us by enrolling in the New England Conservatory which offered a two-year course in "third-stream music," a discipline which seems to concentrate on improvisation in the jazz mode. After one year of this he tried his hand at a number of other things, including being admitted to medical school and not going. He now lives in Woods Hole where he holds a position at the Oceanographic Institution and participates in the design and construction of electronic gear to be used in the deep-sea submersible vessel, the ALVIN. He also plays the piano at the Fishmonger Cafe, a popular local restaurant, and spends some time working on his science fiction novel. George is, in my judgment, a very talented young man but still lacking in direction. The girls are all now on track and it is not hard to visualize where they may be headed. With George I am curious as to how it will all end up.

And then there is Marney. The ties which bind us are of long duration and show no indication of weakening. In an era in which many marriages seem to head toward divorce, ours has lasted for more than forty years and promises to endure. She continues on her career of biochemical research and, with my developing blindness, she has assumed ever-increasing practical responsibility. It is now she who keeps the accounts, pays the bills, calculates the income taxes. In addition, she for many years has done all of the driving and also gives me her elbow as a guide when we walk the dog or go to a restaurant or theatre.

With respect to the book which follows, I dictated the first draft without too much trouble. But I realized that editing was essentially impossible for someone who cannot read. It was therefore understood from the beginning that Marney would take responsibility for editorial revision, and this she has done with great patience. The statements contained in this book are based chiefly upon my personal memory and may therefore be in error. It is not possible for me to consult the literature and check facts. I apologize to the reader for such inaccuracies as have crept in. Marney has undertaken to look upon such matters as seemed most pressing. The book was intended from the first as

memoirs, and what are memoirs if not recalled material including all attendant errors?

Finally, I wish to thank Mrs. Nancy Yellin who typed the original draft, and Mrs. Nancy Hawes who introduced the final draft into her fantastic word-processing machine. I also am indebted to Bernard Talbot and Paul Goldsmith who cheerfully read proof and suggested numerous corrections. It is a humbling thought that this book, which is my life, is now totally contained in the magnetic memory on a couple of flexible plastic discs less than six inches in diameter.

Bethesda, Maryland
Spring 1983

POSTLUDE:

On May 19, 1983, there occurred the most devastating event in my life. After an illness of about 5 days, Marney, who had always enjoyed vigorous good health, never went to hospitals except to have babies, and avoided physicians whenever possible, suddenly died of an overwhelming myocardial infarction. At the time of her death she had completed editorial revision of many of these chapters. I have since asked my good friend, David Denker, of Rutgers days, to complete editorial revision. I find that my contributions to this process are not helpful.

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Chapter I

RUDI

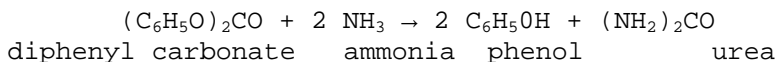
When he returned to the College of Physicians and Surgeons from his visit to the 116th Street Campus of Columbia University in 1937, Rudi Schoenheimer was in a state of profound excitement. This was not at all remarkable. Rudi was generally in an excited state. A fairly typical cyclothymic, his mood was manic most of the time, with only occasional intervening depressions. When manic, he was scintillating, fascinating, and entertaining. When depressed, he was impossible. The present exuberance was well grounded. Over the years immediately preceding, Rudi, his colleagues, and his graduate students had been exploiting the uses of the then novel isotope of hydrogen, deuterium, which had been discovered and made available to us by Harold Urey, of the Department of Chemistry. This isotope made possible a variety of studies in the growing field of intermediary metabolism in which the isotope of hydrogen, stable, that is, nonradioactive, and essentially devoid of toxicity, could be used to label organic molecules and follow them through their metabolic conversions in the body of the intact animal. These studies had served to bring great excitement and enthusiasm to the Department of Biochemistry of the College of Physicians and Surgeons, which is the medical school of Columbia University. They also served to bring personal fame to Rudolf Schoenheimer.

Now Harold Urey had performed his second miracle. As he had previously succeeded in separating the isotopes of hydrogen from nature, he had now succeeded in separating the isotopes of nitrogen. He had prepared samples of this element which were greatly enriched over natural abundance with the rare stable isotope, ^{15}N . The nitrogen of nature is a uniform mixture containing ^{14}N , 99.7 percent and ^{15}N , 0.3 percent. By means of a large and elaborate countercurrent distribution apparatus, two stories high, Urey had succeeded in enriching a sample of nitrogen in the ammonia of ammonium nitrate until the ^{15}N had achieved an abundance of about 30 percent. It can now be told that, in order to feed this greedy tower, Urey personally smuggled many hundreds of pounds of explosive ammonium nitrate in the rumble seat of his coupe through the Holland Tunnel from New Jersey to New York. The transportation of explosives through the tunnel was, of course, explicitly forbidden.

Isotopically enriched ammonia was obviously suitable for the labeling of the many interesting and important compounds of the animal body which contained the element nitrogen. This included amino acids, proteins, purines, and a host of other substances. Today Rudi was bringing home the bacon. He had in a small ampule a major portion of the world's supply of useful ^{15}N . He quickly summoned his associates into his office, and plans were made.

At that time I had completed my medical training, internship, and residency and was working toward my degree of Ph.D. in biochemistry at Columbia. Out of the confusion, I assumed the job of synthesizing isotopically labeled urea from a small portion of the scanty supply of ^{15}N . The excitement was contagious.

This synthesis, like so many others, commenced with a search of the literature, and the literature of organic chemistry was summarized in the great German encyclopedia known as Beilstein's Handbuch. This massive summary of substantially all available knowledge of organic chemistry was the continuing production of the German Chemical Society. The entry under "urea" was very large, but this was not surprising, since historically urea was the very first organic compound ever to have been synthesized. This synthesis by Wohler, in 1828, is taken by many historians as the beginning of organic chemistry. Since Wohler's time, many syntheses of urea had been described and each of these had to be reviewed and considered from the point of view of the demands of the present experiment. Finally a method was encountered described in the German literature by a scientist, whose name I no longer recall, which involved the treatment of diphenyl carbonate with ammonia. The reaction was said to be:



As described in the German literature, the reaction proceeded smoothly when ammonia gas was bubbled into melted diphenyl carbonate held at 100°C, and furthermore, the reaction was said to proceed stoichiometrically. This means that there are no other confusing side reactions, that the product is formed, and the reagents are consumed precisely as indicated by the foregoing equation. One of the charms of this synthesis from my point of view was that the isotope in the nitrogen, which had been concentrated with so much effort by Urey, would not be diluted. The products of the reaction, urea and phenol,

have entirely different properties and are easily separable. After consultation with Rudi, I selected this method as most promising, and a model experiment using ordinary ammonia was set up.

Ammonia gas was generated from a solution of ammonium nitrate and was bubbled through melted diphenyl carbonate. The effluent gas was trapped in acid. To my deep chagrin, apparently no reaction whatsoever occurred. Every last bit of ammonia that was introduced into the system passed right through the diphenyl carbonate without chemical alteration. I naturally tried all likely variations of the procedure, but to no avail, and was finally forced to the conclusion that the German author who had described this method had simply lied. Deeply aggrieved, I so reported to Rudi. "When," he asked me, "was this synthesis reported?" "In 1880," I replied. With a dash of chauvinism, Rudi answered, "In 1880 there was no need for German organic chemists to lie." He next explored with me the details of the original description of the synthesis, and we noted that, whereas I had been working with small amounts of diphenyl carbonate, the original description called for kilogram quantities of reagents. Suddenly Rudi's face broke into a grin: "I can remember when I was a graduate student in Thomas's laboratory in Leipzig. There were hanging high on the walls and covered with dust large copper retorts and other reaction vessels. Glass in those days was not as strong as it is today. Reactions involving kilogram quantities of reagents, particularly when run at elevated temperatures, were usually run in copper vessels. Could it be that copper might catalyze this reaction?" I therefore undertook to do the synthesis once more with the now additional feature that a small amount of copper would be added to the diphenyl carbonate. I found, in the chemical stockroom, a small quantity of finely divided metallic copper which apparently had been prepared to be added to paint to impart a metallic sheen. A pinch of this copper dust was all that was required. The ammonia now generated was indeed quantitatively taken up by the diphenyl carbonate, and urea was formed in the expected yield. The isotope of nitrogen in the original ammonia was evenly distributed between the two symmetrically disposed positions in urea, and this material was subsequently turned over to my colleague, Konrad Bloch, for biological use. It was my first synthesis using ^{15}N .

Rudi's flash of insight in the foregoing episode was the norm and the expected in those days. He was a man of unusual brilliance with a deep insight into natural processes. On many occasions he intuited the outcome of

experiments with remarkable accuracy. During his short career, he performed a relatively limited number of experiments, but he seemed to avoid the false starts and blind alleys which marked the career of many biochemical scientists. He was always hitting pay dirt.

Rudolf Schoenheimer was born in 1898 in Berlin, a scion of a well-established medical family which owned and operated a psychiatric clinic. As a youngster he served in the artillery of the German army during World War I, which was clearly a very traumatic experience. He then went through medical school and proceeded further toward a higher degree in biochemistry, working in Leipzig under the preceptorship of Karl Thomas, an early enzymologist. He never bothered to secure the Ph.D. degree because in those days in Germany a necessary condition for this degree was that the candidate have completely analyzed a mineral. Whereas this requirement did serve to accumulate a vast amount of mineralogical information in the German literature, it was pure data gathering. Devoid of ideas and of imagination, it held no appeal for Rudi, and he therefore declined to conform. At that moment, a job opportunity arose for him. The great Ludwig Aschoff, the dean of German pathologists, professor at the University of Freiburg, had come to the conclusion that the future of pathological inquiry lay in chemistry. Aschoff had long been interested in the abnormalities of the gallbladder and had noted the deposition of cholesterol and cholesteryl esters in the lining of the gallbladder. These he had detected by optical methods. He wished to see these matters pursued at a chemical level. Seeking, therefore, a medically trained chemist, he invited Rudi Schoenheimer to occupy the top floor of the Pathological Institute of the University of Freiburg. This was an offer which Rudi could not decline. He soon was installed and started producing his series of important papers which proved, among other things, that mice can and do both synthesize and destroy cholesterol, that the absorption of cholesterol from the intestinal tract proceeds by way of the lymphatic channels, and that the secretion of cholesterol is accompanied by a minor but analytically distinguishable constituent called dihydrocholesterol. He became involved in a collaborative effort with the famous chairman of the Department of Medicine, Dr. Siegfried Thannhauser. The case involved a patient who had a remarkably high level of cholesterol in her blood. The patient had been referred to Freiburg by a Chicago clinic, and the results obtained were of sufficient interest that Rudi was invited to the University of Chicago for a brief collaboration with the clinical faculty

there. It was while he was passing through New York on his return voyage to Germany in 1931 that I first met Rudi. He was brought to my home by a member of the Columbia faculty, Dr. Erwin Brand. It was Brand's assessment that what Rudi needed more than anything else was a solid and substantial German meal, and it so happened that in our family there was a German cook, Kathe. So a dinner was served of Sauerbrauten and Kartoffelpuffer, which seemed to hit the right spot. Rudi, on cleaning his plate, summoned Kathe out of the kitchen and addressed the bewildered domestic: "As long as there are potato pancakes, we need not worry about the future of Germany." Before the evening was over, it was agreed that I, at that time in my second year at medical school, would spend the following summer months in Freiburg working with Rudi Schoenheimer.

So it came to pass that, in June 1932, I arrived at the railroad station in Freiburg-im-Breisgau, a charming town on the edge of the Black Forest equipped with a medieval market square in which stood a perfect Gothic cathedral. I was duly presented to Geheimrat (privy councillor) Aschoff after a severe instruction from Rudi never to refer to him by any other title than "Herr Geheimrat" or he would not answer.

Rudi put me to work synthesizing fatty acid esters of cholesterol. He also insisted that I master the tedious gravimetric method for the analysis of cholesterol employing digitonin. In addition, I assisted him in making thoracic duct fistulae in dogs which were used to study the route of intestinal absorption of sterols and related substances. I lived a few blocks from the institute in a rooming house run by a Naturheilkundige, a nature healer. My room had a balcony with a view where my landlady would serve me breakfast each day. Room and breakfast, \$8.00 a week.

Aschoff, although formal, proved to be quite congenial. He had a number of foreign students, Americans and particularly Japanese. The institute was bustling with activity. Every morning at eight o'clock we had "Besprechung." This was a conference conducted by the Geheimrat in which he reviewed the previous day's autopsies and all of the literature that had been received by the library during the preceding 24 hours. It was a remarkable tour de force. Then came the daily lecture, always delivered by the Geheimrat himself. The associate professor, Ausserordinarius Buchner, a pathetic image, hoped and prayed that someday Aschoff would be ill or out of town, leaving to him the privilege of giving the daily lecture. This, however, never seemed to happen. Even when he was awarded an honorary degree by the University of Amsterdam,

Aschoff left Freiburg after his morning lecture and returned in time to lecture again the next day. Aschoff was a truly magnificent teacher--a point of some importance, since he attracted a very large audience, and the earnings of a German professor were in good part determined by the numbers of students who enrolled in his course. Being a very successful lecturer, he had become one of the wealthy citizens of Freiburg.

Aschoff took a particular interest in his foreign fellows. He was a member of a drinking and dueling society called the Allemanni Burschenschaft, and he invited all of the foreign students to attend a drinking bout at a Kneipe or students' club, in which the neophytes were required to consume one liter of beer without taking a breath and to sing all of the many stanzas of innumerable drinking songs. After we had absorbed this element of German student culture, Aschoff invited us also to attend the other function of his Burschenschaft--namely, the Mensur. This secret ceremony, still prohibited by the police, was the exercise of saber fighting, prized by German students. Individuals representing two different dueling organizations would compete with each other, with most of their bodies well protected but their cheeks exposed. The duel was a graceless affair in which opponents faced each other and were not supposed to move their feet or flinch. Each round consisted of four slashes with their swords, and with German thoroughness each sword was wiped by the seconds with carbolic acid between rounds. Sooner or later one of the combatants would weaken, his defense would be lowered, and his opponent's sword would slash his cheek. When this happened, the victim immediately called upon his friends for a camera so that adequate pictures could be made to immortalize the event. Most of the bouts appeared to be pro forma with the intent of inflicting or receiving a wound, but occasionally there was a grudge fight where the interest would be somewhat deeper. I recall sitting through this rather dull ceremony with a couple of American fellow students, wondering what it was that we were witnessing, and whether it was possibly related to the growth of the National Socialist Party.

Oh yes, this was the summer of 1932 and Adolf Hitler was on the campaign trail. He even came to Freiburg to make a political address to the assembled students and faculty in the Sportsplatz. I naturally went, since there was limited entertainment opportunity in this quiet university town. I understood little of his highly charged and screaming German but recognized that here was a remarkable showman. He arrived by airplane, then an unusual mode of travel,

in full sight of the assembled crowd. He gave his speech, was duly applauded, and a few minutes after he left the arena, we could see his plane climbing off into the setting sun. It was a stage performance worthy of Richard Wagner.

I took only passing interest in these political events, although Rudi, clearly, was terribly concerned. He was a Jew and recognized quite early that he would have to leave Germany. Since I was a foreigner, he felt, very strongly that I should not be in the neighborhood when the next election day, August 1, 1932, came around. I therefore arranged with a German medical student, Hans Thiersch, to spend a week on the Lake of Constance, which is conveniently on the frontier between Germany, Austria, and Switzerland. We stopped at a charming old inn called Zum Wilden Mann at Meersburg, the site of a ruined medieval castle, complete with moat, dungeon, wine cellar, and mill wheel. When the caretaker learned that I was American, he tried to sell Schloss Meersburg to me for \$50,000. We spent a pleasant few days exploring the lake in Thiersch's Faltboot, a cleverly constructed kayak with a rubberized canvas skin. When the election was over, we learned that Hitler had done poorly, and the consensus was that he had passed his political peak. We had planned to descend the Danube from the town of Donaueschingen to Vienna in the kayak but were discouraged by the almost continual rainfall. We therefore parted company and I proceeded alone to Vienna, thence to Zagreb, Yugoslavia, where my sister Margaret was living with her husband Maximilien Vanka, who was a professor of painting at the local university. Margaret had recently given birth to a gorgeous girl baby who served as a model for me and my very newly acquired Leica camera.

On my return to New York I entered my third year of medical school at the College of Physicians and Surgeons (P & S), still clinging to the notion that upon attaining my M.D. degree I would return to Freiburg to secure a Ph.D. in biochemistry with Rudi. However, this was not to be. By December 1932, Rudi had come to the United States under a fellowship from the Josiah Macy, Jr., Foundation and had transferred his research base to the Department of Biochemistry at P & S. At about this time he married a very gifted and vivacious biologist, Salome Gluecksohn, and soon they were settled in the New York area. I continued to see a good deal of the Schoenheimers over the ensuing years while I finished my medical training. Clinical medicine and the medical specialties excited me far less than had the basic medical sciences. The third year was devoted chiefly to clinical clerkships on the wards of Presbyterian and other affiliated hospitals, while the fourth year was spent largely

in the several outpatient departments. My instructor in medicine chanced to be Dr. Dickinson Richards, who subsequently shared the Nobel Prize with Andre Cournand for their studies in cardiac catheterization. Dick Richards was a charming, gentle, and scholarly man and a very considerate teacher. The chief character of the Department of Medicine at that time was, of course, Robert Loeb, a brilliant and knowledgeable physician endowed with an extraordinary memory for facts and faces and a very keen insight into all medical matters. Although he was an excellent teacher, he unfortunately could not resist dressing down students who performed ineptly or responded stupidly. He was held in terror by many of my classmates. I, however, always found him to be delightful and very helpful. In fact, for the many years that followed, I made no important career decisions without consulting with Bob Loeb, and his advice was always thoughtful and good.

The subject of surgery I found devoid of any interest. This, I realize, was a disappointment to my father, who had fully expected that I would follow in his footsteps and ultimately inherit his prosperous surgical practice.

Upon graduating from P & S, I entered into an internship-residency at Bellevue Hospital on the Third Medical Division. At that time, Bellevue was one of the largest hospitals in the world and by all odds the largest hospital in New York City. It was located on First Avenue and faced the East River between 26th and 31st Streets. It was, of course, a member of the system of city hospitals and many of its buildings were very old and in poor condition. It housed about 2,400 beds, a grossly inadequate number of nurses, and a profusion of cockroaches. The medical wards were large, sunny rooms, each containing 26 beds, with a view of the East River. However, this did not limit occupancy to 26 patients. During the winter influenza seasons, a row of cots would be set up between the two rows of beds and the population of a ward might well rise to 50. An intern was assigned to each ward. To each, pair of wards there was assigned a junior house officer, and to all four medicine wards there was a supervising senior house officer. The progression of duties was that the first year one served as an intern 6 months on medicine and 6 months on surgery. The next portion of the appointment, lasting 18 months, was made up of 6 months on pathology, 6 months as junior house officer, and 6 months as senior house officer. In my own case, promotion to senior house officer was accelerated because the man directly preceding me developed pulmonary tuberculosis, an all-too-frequent ailment among house officers at Bellevue Hospital at that time.

The pace was truly grueling. The intern, in addition to being on call every day, was also on call every alternate night. The house officers, however, were given 3 of 4 nights off duty. Of course, we all lived in the hospital in small and modestly furnished dormitory-type rooms. Since no double rooms were provided, marriage was forbidden to interns and residents. We often worked around the clock without ever getting to our quarters. The meals provided were simply atrocious, but the hospital did supply us with white pants and coats, and we were paid the handsome stipend of \$7.50 per month. We all worked very hard, indeed, harder than I have ever worked at any other time in my life, and we were all in a chronic state of exhaustion. The learning-teaching experience, however, was very intense, and I doubt if I ever acquired more information in so short a time than I did during my stay at Bellevue Hospital. The visiting staff on the Third Division, which comprised the Department of Medicine of the New York University Medical School, was active, loyal, and of very high quality. I shall never forget Dr. Joseph Connery, in charge of hematology, who was even at that time assaying for the Lederle Company various preparations of liver extract for the treatment of pernicious anemia. Dr. Elaine Ralli took meticulous care of her precious diabetic patients, while gentle Dr. Clarence de la Chapelle provided a tidy and systematic differential diagnosis of diseases of the heart. Dominating the service was the dean of the New York University Medical School and chairman of the Department of Medicine, Dr. John Wyckoff, a dynamic man and a powerful leader, whose suicide shortly after I had left Bellevue Hospital saddened us all. It appears that Dr. Wyckoff, in his role as a consultant to one of the life insurance companies, had failed to detect a systematic fraud which was being practiced in New York City. Unethical physicians were coaching derelicts in the signs and symptoms of myocardial infarction and were then feeding them toxic quantities of digitalis to produce arrhythmias and other abnormalities in the electrocardiogram. Thus primed, these people would then stagger in to a doctor's office complaining of chest pain and would be diagnosed as having myocardial infarcts. Having previously purchased disability insurance, they could then return to normal life and collect for their purported disability. Dr. Wyckoff had failed to suspect this fraud, and when it was finally discovered he found the shock overwhelming.

I finished my residency on December 10, 1936. I can fix the date precisely because I had three weeks of annual leave due to me and my appointment

normally terminated on the last day of the year. To celebrate my release from Bellevue, my sister Margaret had arranged a party in her studio apartment on Central Park West. There we sat down to a fine dinner with my brother-in-law Maxo, my niece Peggy, then about 4 1/2 years old, and other company. Later in the evening we turned on the radio to hear Edward VIII abdicate from the throne of England in order to remain true to the woman he loved. As may be imagined, after this dramatic and historic announcement there was lively conversation in Margaret's living room. One of the guests commented that he had encountered Edward VIII, then Prince of Wales, on the French Riviera a few years earlier, and what a shame it was that the Prince drank so much every night. At this point my diminutive niece piped up, "Oh he shouldn't do that!" We turned to the little girl to ask, "Why not?" Out of the babe's mouth came the unexpected response, "Because if he drinks a lot at night he will make pee-pee in his bed."

The next day I sailed for Naples where I met my mother. We traveled thence to Taormina, where we chartered a car and over the next few weeks made a circle tour of Sicily.

When I returned to the United States in January of 1937, I entered the graduate school of Columbia University and spent most of the next year taking courses in physical and organic chemistry and in mathematics, and preparing to qualify as a Ph.D. candidate in biochemistry. It was during these studies that I encountered Marjorie Roloff, called Marney, on the steps of Havemeyer Hall, which housed the Department of Chemistry. We were fellow students in a physical chemistry course. This encounter led to friendship and ultimately blossomed into marriage.

Upon completion of my coursework, I returned to the Department of Biochemistry at P & S, where I went to work on my dissertation research under the guidance of Rudi Schoenheimer, now an assistant professor in that department. At that time, the Department of Biochemistry at P & S was probably the leading center for biochemical research in the United States. This was largely due to the benign guidance of its chairman, Hans Thatcher Clarke. Although an American by birth, Hans Clarke had received most of his training in England and in Germany. He was educated as an organic chemist and had served his time in the laboratories of the great Emil Fischer in Berlin and as the director of organic chemistry at the Eastman Kodak Company in Rochester. Whereas his knowledge of biology was limited, he compensated for this by wisdom in

classical organic chemistry. This was exemplified in his extraordinary skill in the identification of organic substances by their odors. This we tested on many occasions, and he rarely failed us. Historically, it is noteworthy that it was his delicate sense of smell which first identified the thiazole ring in the structure of vitamin B₁, which was being isolated and purified at that time by Williams and Waterman, with the technical assistance of my fellow graduate student, Samuel Gurin. Hans Clarke was a large man of distinguished appearance. He favored a British regimental mustache and had a ready smile. The leadership which he gave his department was based largely on his remarkable tolerance. Taking advantage of his familiarity with German culture and the German language, he collected in his department many German- and Austrian-trained scientists who were then seeking haven. These included the microanalyst and steroid chemist Oskar Wintersteiner, the expert on mucopolysaccharides Karl Meyer, the protein chemist Erwin Brand, the nucleotide chemist and philosopher Erwin Chargaff, and the student of sugar metabolism Zacharias Dische. These, together with the solidly American-trained biochemists Edgar G. Miller, G. L. Foster, and Robert Herbst, were the core of the faculty. It was into this group that Rudi Schoenheimer had entered a few years earlier, supported initially by a grant from the Josiah Macy, Jr., Foundation. Upon his arrival, Rudi pursued his earlier interests in steroid metabolism, but then an event occurred which provided him with a remarkable opportunity--and Rudi was not one to let opportunities slip from his grasp.

Harold Urey, at that time a rising young professor of chemistry on the Columbia College campus, had noted an asymmetry in the so-called ghost lines of the spectrum of hydrogen from various sources and deduced that this might be due to the existence of a very minor component in natural hydrogen--namely, an isotope of hydrogen. He had learned early that electrolysis of water tended to increase the abundance of this minor isotope, and he therefore studied the water which remained in old, used storage batteries. He discovered, to his delight, that the new component was very much increased in concentration in such water. Starting from these modest beginnings he soon was able to produce highly purified heavy water, deuterium oxide, which differed from traditional water--namely, hydrogen oxide, by a replacement of the hydrogen of mass 1 by isotopic hydrogen, deuterium, of mass 2. Deuterium oxide was remarkably similar to ordinary water in many of its properties. It was, however, appreciably more dense and had somewhat different optical properties.

Electrolysis of deuterium oxide readily yielded deuterium gas, which was also remarkably similar to hydrogen gas in most of its properties and reactions. It was immediately appreciated that deuterium, if it could be introduced into any molecule in place of hydrogen, might serve as a label whereby the progress of the molecule through any transformations could be followed. It was Hans Clarke, I believe, who introduced Harold Urey to Rudi Schoenheimer, and out of that introduction there developed a remarkable piece of biochemical history. Harold Urey placed at Rudi's disposal 6 ml, approximately one teaspoonful, of precious deuterium oxide which he had prepared; and Rudi and his colleagues, practicing enormous economy, extracted from this initial gift a number of very important biochemical advances and a number of widely studied papers. The excitement in the laboratory was intense. It was at this time that I appeared as a graduate student. Rudi was already collecting a group of collaborators with whom his name has become associated. These included David Rittenberg, Albert Keaton, Sarah Ratner, and Konrad Bloch, and a most cherished technician, Morris Graff. Shortly after I joined the group, Marney also moved from the Columbia Department of Chemistry at 116th Street to 168th Street.

The Department of Biochemistry at P & S was remarkable not only in the extraordinarily high quality of the research activities of its faculty but also in its architectural arrangement. All the graduate students shared laboratory space in one huge laboratory. Thus, in addition to those who worked for Schoenheimer, we were put into intimate and daily contact with Lew Engel, Dave Shemin, Norm Weissman, Marge Anshel, Doris Blumenthal, Bill Stein, Henry Hoberman, Aaron Bendich, David Sprinson, Earl Evans, Sam Gurin, and many others, and also a number of transient fellows including Kits Van Heyningen and Sune Bergstrom. This arrangement had, I believe, a great deal to recommend it, in that we all became more or less familiar not only with our own research activities but also with those of a number of our contemporaries. We all participated in an active and sometimes combative weekly journal club, and at one time or another most of us had some responsibilities in the teaching of biochemistry either to medical or to dental students. I soon became what would today be called a teaching assistant in the medical biochemistry course, a task which I came to enjoy hugely, being almost the only M.D. in the department. I believe that I was able to bring to this course a level of significance to the medical students which was otherwise lacking. The innumerable relationships

between biochemical phenomena and problems of health and disease were becoming increasingly apparent at that time, and I assumed the responsibility for presenting these relationships to the student body.

My own dissertation research had to do with the biological interconversions of fatty acids, the major ingredients of all animal and vegetable fats and oils. These long straight chains of carbon atoms, each bearing hydrogen atoms and terminating in an acidic carboxyl grouping, vary both in length of chain and in numbers of hydrogen atoms. We were able to show that in the case of palmitic acid, C-16, the chain is not only degraded to C14 and C12 but is also elongated to C-18, always by two carbon atoms at a time in the body of the living animal. We furthermore showed that two hydrogen atoms could be removed by biological processes. In addition, I was able to demonstrate that the corresponding alcohols and hydrocarbons could be oxidized to the level of fatty acids. Whereas some of these interconversions had long been suspected, it remained for the application of the isotopic tracer method to demonstrate conclusively that they actually occurred and to provide a measure of the extent of their occurrence. This was done by replacing some of the hydrogen atoms attached to the carbon skeleton of fatty acids by deuterium, a transformation which affected minimally the properties of the fatty acids. We could then isolate suspected products and analyze them for deuterium content, an analysis performed at that time by the extremely meticulous and tedious falling-drop method. This was a very refined means of estimating the density of a very small globule of water which was in turn secured from the combustion of the organic molecule to be analyzed. The drop, delivered by a precision pipette into a medium of density slightly less than that of water, was allowed to fall freely, and its final rate of fall was determined. This was then related to the abundance of deuterium in the water. The conduct of hundreds and perhaps thousands of such analyses required considerable perseverance and great attention to detail. Any contaminant in the water would introduce serious error in the analytical result and might lead to false conclusions. Therefore all water samples had to be redistilled and their density redetermined. Also, it should be recalled by contemporary readers of this volume that all of this happened long before chromatography was available for the separation of fatty acids. Individual fatty acids had to be separated one from another by tedious fractional distillation conducted on the very small amounts of material which could be recovered from the liver or organs of a mouse or a rat. All of these

procedures had to be modified to meet the peculiar needs of the current experiment. Ultimately, sufficient data were assembled to permit firm conclusions and the composition of a doctoral dissertation. This was done under the ever-watchful eyes of Rudi Schoenheimer and Hans Clarke, each making, or trying to make, his contributions not only to the substance of the paper but to the choice of words. Rudi, for whom English was clearly a second language, favored literal translation from the German. Thus, in the American literature we say the compound melted "with decomposition." The corresponding German phrase is "unter Zersetzung." This, Rudi would literally translate into "under decomposition," a form which he favored strongly over the accepted American form. Similarly, he favored the phrase to describe a reaction which was run at elevated temperature, "in the hot." When I argued this construction, he countered with, "You frequently say 'in the cold'; why can't you say 'in the hot?'" There was no denying the logic of his case. I recall my chief battle with Hans Clarke had to do with the phrase "1 1/2 grams" as against "1 1/2 gram.," I felt that any quantity greater than one commanded the plural, while Clarke favored the view that any quantity less than two was singular. The problem was ultimately resolved when we both recalled that in the journal both gram and grams are represented by the letter g, eliminating the need for a decision. I am sure that up to the time of his death Clarke believed that he was right in this particular controversy, while I am certain that he was not.

The rules of the department required that the dissertation be published in what was then the only important journal for such publications in the United States, the Journal of Biological Chemistry. Then followed the awesome formality of the oral defense of the thesis, which took place in the Low Library at Columbia College. Here I was confronted not only by members of my own faculty at P & S, but also by representatives of the Chemistry Department at Columbia College, including the formidable Harold Urey. Fortunately I survived this ordeal, and at the following commencement in 1940 I was awarded the Ph.D. degree. The very next day I had lunch with my old friend and tutor from Harvard College days, Dr. Frank Fremont-Smith, who was at that time the medical director of the Josiah Macy, Jr., Foundation. He inquired into my future research plans and pointed out what I had never really seriously considered, that conducting research costs money. He suggested that I apply for funds to his foundation and I therefore prepared a very brief application for funds totaling, if I recall correctly, \$2,400 for the next year. This would permit

me to pay the salary of a full-time technical assistant and to purchase such material and supplies as I needed. Hans Clarke assigned a fine laboratory module to me which I occupied for the next 7 years.

In my new and relatively independent condition I continued to meet with Rudi on a daily basis. I kept informed of his activities and he kept informed of mine. As mentioned earlier, when isotopic nitrogen, ^{15}N , was provided by Harold Urey, Rudi had the first chance to use this material and expanded his studies to include different nitrogen-containing substances of biochemical interest, particularly the amino acids. In collaboration with Sarah Ratner, Dave Rittenberg, and others, he explored a variety of interconversions of amino acids and started to elucidate some of their metabolic pathways. He developed the concept of protein turnover and started formulating his ideas which were finally assembled in his book, The Dynamic State of Body Constituents (a series of lectures he composed during the last year of his life and which were delivered posthumously by David Rittenberg at Harvard Medical School). He continued as a brilliant and creative scientist, always generating novel ideas and with uncanny instinct selecting the right experiment to be performed at each moment. Had he lived longer he would certainly have accumulated all of the highest honors which are available to a biomedical researcher. He was, however, fatally flawed.

Those of us who knew him well were fully aware of his preoccupation with suicide. I recall that the very first time I met him, at my home in 1931, he discussed at some length how he had almost committed suicide in a fit of depression while visiting in Chicago. On many occasions thereafter he discussed this prospect. He was impressed by the fact that several members of his immediate family had committed suicide, and he stated from time to time that it was this family taint which discouraged him from having any children. I tried to direct him to psychiatric help, but he had had an unfortunate experience while in Germany which had soured him for life on psychiatrists.

He did have occasional bouts of deep depression, often precipitated by what appeared to be trivial events. I recall that on one occasion he was unable to find a particular spatula which he wanted at that moment in the laboratory. He exploded with some violence, charged all of us with stealing his favorite spatula, and stormed out of the laboratory. He was not seen again for 3 days, after which he arrived unshaven and disheveled. He was not able to give a clear account of all of his actions but apparently had spent much of the

intervening time sitting in a movie theatre. Soon his good nature was restored and he reverted to his more usual manic or hypomanic mood.

On February 7, 1941, Marney and I were married, and Rudi was delighted with the role of Cupid which he fancied that he had played. He was full of advice and presented us with a very handsome gift, a fifteenth century manuscript missal on vellum, which he had discovered in a bookshop in Paris many years earlier and which had been bound in pigskin by his old friend, the daughter of Ludwig Aschoff. That summer, Rudi went west and spent several weeks on the Berkeley campus preparing the draft of a series of lectures which he was to give at Harvard the following fall. Marney and I saw him briefly in California in August. What transpired after that is a little uncertain. We know that he drove home across the country with a University of California student and that there was an automobile accident in which Rudi purportedly was injured. On his return to New York he was noticeably upset. Marney and I were moving into a new apartment house on 158th Street and Riverside Drive, and one evening we had Rudi for supper. He was at this time already separated from Salome and was looking for quarters for himself. He liked the location of our apartment house, which was within walking distance of P & S, and he asked to meet the manager to inquire whether there were apartments still available there. The following day, September 11, 1941, we were shocked to learn that Rudi Schoenheimer had committed suicide in the tradition of Victor Meyer and Emil Fischer --namely, by the ingesting of potassium cyanide. At the time that he was visiting our home, he had already composed suicide notes to some of his friends, including us. These were delivered in the days following.

The death, of course, saddened us enormously. It was a particular problem for Marney, who was at that time part way through her own Ph.D. research program and now was lacking a preceptor. Happily, Hans Clarke obliged and nominally became a preceptor, although the details of the problem were, I believe, never entirely familiar to him. I was, I hope, able to give Marney some support and assistance. Ultimately she completed the program and received her Ph.D. in biochemistry from Columbia University. As will be seen in subsequent chapters, she has been a working biochemist ever since.

To me, Rudi's suicide was not entirely unexpected. To most of his acquaintances, however, the death was a very great surprise. Hans Clarke, for instance, commented that he saw no reason for suicide since Rudi's career had been progressing so famously.

Chapter II

EARLY TIMES

I was born on May 31, 1909. My father, Dr. Dewitt Stetten, was at that time a blossoming young surgeon practicing at what was then called the German Hospital, which changed its name to Lenox Hill Hospital during World War I. My mother, Magdalen Ernst Stetten, was delivered of me at her home, an apartment on Madison Avenue in New York. This event had been preceded by about two years by the birth of my sister, Margaret, which completed our immediate family.

I knew only two of my grandparents. One was my father's mother, then widowed, who lived in an apartment far uptown on Edgecomb Avenue. She, although American by birth, was of German parentage and her deceased husband was also German. He was, I was told, an importer of fancy groceries from Europe. My mother's father, Carl Ernst, also resided in New York, much of the time at the Hotel Ansonia at 73rd Street and Broadway. His wife, Sarah Bernheim, had died of tuberculosis some years before my birth. The Bernheim clan was vast. My maternal grandmother was one of 8 siblings, offspring of a marriage of first cousins, all of whom married and several of whom established large families, my mother being one of 14 first cousins. Characteristically they were all affluent and successful. The one member of the older generation whom I remember most vividly was my great uncle, Eli Bernheim. In early life, he was a partner in a shirt company which placed the low bid for a contract to provide shirts to the United States Army at the time of the Spanish American War. When he recalculated his bid, he discovered that he would necessarily lose money on the contract. Taking a small chance of being detected, he had two inches cut off of the specified length of each shirrtail. According to his version of the story he turned a tidy profit on the deal. My fantasy of this yarn was a picture of Teddy Roosevelt leading the Rough Riders up San Juan Hill, shouting "Charge!" while his followers were all tucking in their shirrtails. Thus did my Uncle Eli impact on American history. In later life, Uncle Eli served as President of Manufacturers Trust Co., and lived sumptuously on Park Avenue, surrounded by a collection of Corot paintings and tended by his valet. It was not until after his death that his expectant

beneficiaries learned that, in fact, he had long been living on credit and owed even his valet a year's back wages.

My Ernst grandfather hailed from Pilsen, then in Bohemia, now in Czechoslovakia. He had come to this country as a young man with the standard intention of avoiding induction into the military forces of the Emperor of Austria. He joined an older brother in Uniontown, Alabama, where he prospered and soon became co-owner with his brother of the village store. Here he speculated in cotton futures and sold dry goods to the local farmers. Having prospered in his speculations, he and his brother moved to New York to enter the real estate business where, throughout the rest of their lives, they alternated between prosperity and bankruptcy. By the time of my birth, Carl Ernst was living in retirement, devoting his major efforts to the playing of pinochle, a game which he tried a number of times to teach to me, his only grandson at the time. I remember him chiefly as a weekly guest at our home for Sunday dinner, which in those days was an imposing affair with five, six, or seven courses.

My father had been educated in the public school system of New York City and earned upon graduation a coveted Pulitzer scholarship, which provided him with four years of collegiate education. Since in those days a baccalaureate degree was not required for admission to medical school, and since he had already determined upon his career, he circumvented a baccalaureate education and applied his scholarship to four years at the College of Physicians and Surgeons, Columbia University, where he graduated in 1901. American physicians seeking training in surgery in those days routinely sought opportunities in Europe. My father spent the next two years in the city of Prague as Assistent to the great surgeon von Mikulicz.

My parents were engaged throughout this 2-year period and were married shortly after his return to the United States. He secured a staff position at the German Hospital under the preceptorship of Dr. Frederick Kammerer, which must have been regarded as a very desirable position. My father's surgical practice grew and the family prospered. Shortly after I was born the family moved into a brownstone high-stoop house at 115 W. 87th Street, which still stands. The basement contained a dining room toward the front, a kitchen to the back, and a very small fenced-in back yard. The first floor, which was at the head of the high stoop, was the doctor's office. The waiting room was toward the front, the office was in the center, and the examining room projected out to the rear. The next floor contained my parents' living room,

bedroom, and bath, while the top floor was devoted to Margaret and me, with the center room occupied by a young German woman, Lina Baumann, known to all of us as Linchen. She had come from the Rhineland to this country at about 18 years of age and throughout her long life had but one employer--namely, the Stetten family. Initially she was retained to assist in the care of my sister and to participate in running my father's office. When I was born, she took me on as an additional responsibility. It was she who determined that for me to be called Dewitt Junior was absurd. She said: "Devitt, Devitt, was fur eine Nahme ist das?" Since my sister's name was Margaret, for which the German diminutive is Gretel, she decided that we should be Haensel and Gretel. Thus, to all who came into the home, I was known as Hans. She furthermore undertook to teach both Margaret and me German, and indeed I have been told that I spoke German before I spoke English. We certainly learned a number of German songs and poems, many of which I still remember. Linchen adopted our entire family and continued to work for and with us until she died at the approximate age of 80. Over the years she transferred her major affections from my father to me and finally to my son, George. She never married, had few outside contacts, and devoted herself entirely to our affairs. She taught herself typing, prepared my father's income taxes, and pursued his delinquent accounts receivable. She mended our clothes and nursed us when we were sick, which was not often. I have not encountered among my acquaintances any comparable stories of dedication and devotion.

My parents set a very high store upon education. I was therefore sent at a very early age to a local private kindergarten and school called The Alcuin School, named for Charlemagne's pedagogue. This was within walking distance of our home, in the block between Columbus Avenue and Central Park West. Our house lay between Columbus and Amsterdam Avenues. As soon as Margaret and I mastered the complexities of crossing Columbus Avenue with its noisy elevated railroad, we were allowed to walk to school together each morning. Columbus Avenue was a fascinating place. Besides the elevated trains which gave the Avenue a somber complexion, there were many other interesting sights. There was, for instance, the jewelry and watch store owned by a Mr. Ernst (no relative). His chief fascination lay in the fact that he had once been shot by a would-be burglar and he carried the bullet as a fob on his watch chain. This he would display to me on many occasions. From time to time I would visit, first in the company of my father and later by myself, at Dominic's Barber

Shop, which was on the other side of Columbus Avenue. Dominic was a genial Italian with a great love of the opera. Whenever Verdi was performed at the Metropolitan, Dominic would be in one of the cheap seats. Then the next day, while performing his tonsorial operations, he would sing the tenor arias at the top of his lungs. It should be remembered that these were the days of Enrico Caruso and Beniamino Gigli. We deemed it a privilege to have our own local Caruso available to help pass the tedium of a haircut. At a somewhat later date, the store on the southwest corner of Columbus Avenue and 87th Street was taken by the Brunner Brothers offering a new and fascinating line of goods --component parts of radio sets--but more of this later.

As the family prospered and as the children grew up, it was determined that our continuing education should be carried out at the Horace Mann School. This institution on Broadway at 120th Street was the experimental school associated with Teacher's College of Columbia University, and it was clearly a high-quality operation in modern educational methods. Margaret and I learned to make the trip from the 86th Street station of the Broadway Interborough Rapid Transit, getting off at 116th Street and walking the four blocks to school. The trip was not without interest. We purchased our little green tickets at 5 cents each from the man in the cage, and these in turn we deposited into a tall glass box where yet another man, operating a lever, chopped up the tickets. I suppose this system was devised to minimize embezzlement. Soon it was to be replaced by turnstiles into which one could drop the nickel directly and then, after passing through the turnstile, inspect the coin under magnification. This system was designed to discourage the use of slugs, washers, and other objects which approximated a nickel in size. The IRT had many features fascinating to a youngster, such as the car cards with their flamboyant advertisements and the derelicts and drunkards occasionally encountered. Over the ensuing years I became thoroughly discouraged with subway transportation in New York and have vowed in my later years never to use this system if it can be avoided.

During World War I, 1917-18, my father was commissioned as a captain, later major, in the Army Medical Corps, and was assigned to operate at base hospital No. 1, a collection of wooden one-story buildings constructed on a field facing Montefiore Hospital on Gun Hill Road in the Bronx. At about this time our family acquired its first automobile, a large green Buick touring car, which seated at least 7 persons and had a roof that folded completely down. With

the car came a chauffeur, Albert by name, since neither of my parents could master the skill needed to drive a car. Often when my father was driven to the Bronx in the morning, he would deliver Margaret and me to the Horace Mann School, en passant. Horace Mann School was a large and solidly built brown-stone building, coeducational through the first six grades. It was during my years there that I first developed a friendship with Jerome D. Frank, who passed with me through grade school, through high school, and through college. Jerry was precisely one day older than I and we immediately became firm friends. I may add that this friendship has lasted up to the present. He is now Emeritus Professor of Psychiatry at the Johns Hopkins Medical School and lives in Baltimore. Apart from his contributions to psychiatry, which include the introduction of group therapy, he has made an important career out of his love of peace and his hatred of weapons. He has persevered as an active member and lay preacher of the Ethical Culture Society and has developed a large following, particularly among members of the younger generation, who support his notion that war is the poorest possible way of solving problems. I am proud to have been his friend over a period of at least 60 years.

Another important event which occurred during my years in the Horace Mann grade school was my attendance at the meetings of the Science Club, which was established by Dr., then Mr., Morris Meister. Morris Meister was at that time a graduate student at Teachers College and was developing his dissertation designed to demonstrate that science education could usefully be initiated far earlier than was then current practice. In order to explore this thesis he established a science club, drawing upon students from the classes at Horace Mann and meeting on Saturday mornings. Jerry Frank and I were both members of this club and thoroughly enjoyed the experience of performing experiments for each other's bewilderment during these Saturday morning sessions. The science that Morris Meister taught was not the didactic but rather the experimental sort. Whether this experience had an important influence on my subsequent choice of career, I cannot state with certainty. I can, however, note that Dr. Morris Meister moved on to establish the Bronx High School of Science, a school which has been a leader in developing young scientists. Now, many years later, I sometimes attend the annual banquet at which the Westinghouse Science Scholarships are awarded, and it is impressive how many of these bright youngsters derive from the Bronx High School of Science. Much later,

as a practicing biochemist, I encountered the gifted biochemist, Alton Meister, and learned that he was the son of my old preceptor.

Although the Horace Mann School made claims to progressive education, we were in fact thoroughly drilled in reading, writing, and arithmetic. We had spelling lists and spelling bees and were given abundant homework. We read extensively and were encouraged to use the well-stocked school library. While still in grade school, Margaret and I were given private lessons in French by a madame whose name I no longer remember but who smelled, as I vividly recall, of a somewhat rancid perfume. It could be that my disability in the French language as compared with my fairly reasonable recall of German is related to my distaste for Madame's scent. We were, in addition, both introduced to the piano. Whereas my father was essentially tone deaf, my mother was a skilled pianist and had studied voice when younger. It was at her insistence that Margaret and I practiced the piano for about half an hour every day and continued to take lessons for a number of years. I must admit, however, that neither of us ever became competent performers. Our musical education was supplemented by attendance at concerts on Saturday mornings at Aeolian Hall. Here Walter Damrosch conducted the New York Symphony Orchestra in concerts directed toward the young and taught us both the appearance and the voice of each orchestral instrument. We also were taken to many piano concerts, and I was privileged to hear Rachmaninoff, Paderewski, and particularly Joseph Hofmann, who was the teacher of my favorite piano teacher, Claire Svehenski. By this tenuous connection I was taken backstage and introduced to the great man and secured his autograph in my copy of his autobiography.

Our home was a fairly literate one. There was an extensive library featuring chiefly sets of the standard Victorian authors, such as Dickens, Thackeray, Macaulay, and Stevenson. My mother's literary interest ran to Emerson, with a taste for poetry, especially the Victorian British poets, and such American poets as Bryant, Longfellow, and Whitman. Reading aloud was a common activity and the children were expected to commit poems to memory. I found this activity relatively easy, and I recall once earning \$5 by wagering with my father that I could memorize all seventy stanzas of the long Macaulay poem entitled "Horatius at the Bridge."

Lars Porsena of Clusium
By the nine Gods He swore
That the great house of Tarquin
Should suffer wrong no more.

By the nine Gods he swore it,
And named a trysting-day,
And bade his messengers go forth,
East and west and south and north
To summon his array.

East and west and south and north,
The messengers ride fast, . . .

Now, some 65 years later, I can still recite portions of this "Lay of Ancient Rome."

I recall another episode which relates to the reading of poetry aloud in our family group. My sister, on one occasion, called upon my parents to read again to her the poem about the girl who vomited the ribbon. This curious request brought nothing but puzzlement from my parents who could not recall such a poem. It was not until the end of the following December when we had a traditional reading of Christmas verse that this puzzle was solved. With the opening line, "T'was the night before Christmas and all through the house, not a creature was stirring not even a mouse, Margaret became quite agitated. "That's it, that's it," she cried. Finally the reading progressed to the deathless line, "I ran to the window and threw up the sash."*

Apart from his medical and surgical interests, my father had wide-ranging curiosity and was by instinct a collector. He collected etchings by Anders Zorn. He had a number of ancient books on medicine and a particular interest in Persian ceramics of which he acquired some fine examples. He enjoyed auctions, deriving, I believe, deep satisfaction in shrewd bidding. He was a surgeon of the old school, something of a prima donna in the operating room as well as at home. He had a temper and all of us stood in dread of it. By way of compensation, my mother had become very meek and subservient. In keeping with established tradition, my sister identified largely with my father, while I was far closer to my mother.

After completing the sixth grade at the Horace Mann School, 120th Street and Broadway, I was admitted to the Horace Mann School for Boys, which was located on a hill overlooking Van Cortlandt Park, at about 246th Street in the

*For the benefit of younger readers, the word sash was used to describe a broad ribbon which young women wore around their waists as a sort of belt, and also means the movable part of a double-hung window.

Bronx. The girls continued their education at the downtown institution but the boys now went to the end of the Broadway subway line. Each school day morning for the next six years I would travel by local subway to the 96th Street station and there await the Van Cortlandt Park Express which departed that station at 8:30 a.m. It was about a half-hour run to the end of the line at 242nd Street. My schoolmates and I always collected in the front car of the train where we could find seats. It was during these years that I learned something of the game of chess, which we played almost daily on small portable chess boards while in transit. I was only a moderately successful player, and after completion of high school I do not recall that I ever played seriously again.

The boys' school was a new world. It was housed in an austere rectangular gray fieldstone fortress, standing beside a large athletic field with a track around it. Across from the school was a large gymnasium and swimming pool. Whereas in the lower school the faculty was predominantly female, at the boys' school the world was almost as male as Mount Athos. The only woman teacher was Miss A. Berdena McIntosh, who taught introductory Latin. The only other women whom I recall were the librarian, Miss Brainard, and the secretary to the principal, Mrs. Dodge, who was the wife of the teacher of Romance languages. The principal, or headmaster, in my time was Dr. Charles Tillinghast, a dedicated and serious pedagogue, whose breadth of knowledge permitted him to replace any teacher in any department. Discipline was quite strict. Homework loads were very heavy, requiring several hours every evening. I took a full load with five consecutive years of Latin, four years of French, and all the mathematics and science that the school offered.

A feature of the school, derived from its Teachers College tradition, was that one learned through doing. This meant that the school had a very well-equipped carpentry shop with many fairly sophisticated power tools, and a manual training teacher, John Mulholland. I really became interested in woodwork and soon set up a modest shop in the small room which adjoined my bedroom at home. John Mulholland, in addition to his skills as a woodworker and metal worker, was also a very gifted magician. During my school years I was a shy and somewhat withdrawn boy, not much interested in sports and slow to make friends. This gave my parents some concern and they discussed the problem with a psychiatrist friend, Dr. Menas Gregory, of Bellevue Hospital. It was Dr. Gregory's suggestion that I should be taught to do something that the

other boys did not and could not do. After some consideration, it was determined that I should be sent to Europe one summer, 1924, in the company of John Mulholland, and it was in the course of that summer that I became seriously infected with a love of magic. I took this hobby very seriously, developing considerable manual skill and acquiring a substantial collection of equipment. I soon was giving shows, first for friends at children's parties, later for a fee at assemblies of adults. John took considerable pride in me as a pupil and years later admitted to my wife some disappointment in my selection of biochemistry as a career. "He might have made a good magician," John told Marney on the occasion of their first meeting. In later life, John Mulholland devoted all of his considerable skill and energy to the profession of magic. He assembled a fine library of books on the subject, both new and ancient, and was in all ways a magician's magician. He is very largely responsible for my two most enduring hobbies, conjuring and carpentry.

Education at the Horace Mann School for Boys was a serious business. Whereas there was a very small dormitory, the majority of students lived at home. The school, however, did have many of the characteristics of a college preparatory school, and virtually every graduate went to college. School lasted every day from 9 to 5, which include a 2- to 3-hour sports period every afternoon. The faculty addressed the students by their last names, and the principal, Mr. Tillinghast, was always referred to as the headmaster in the British tradition. Discipline was quite strict and the punishment for infractions was usually "laps around the track." The director of athletics, a humorless man known as "Ump" Tewhill, always started his sessions with sitting up exercises. We were required to select at least one team activity. Baseball and football were beyond me because of my extreme myopia, although I did play tennis in a mild way. I usually favored soccer because the teams were large and my non-participation might pass unnoticed. Swimming was, as I recall it, a requirement in the sense that one had to swim two lengths of the pool in order to graduate.

The high school course in mathematics was at the time remarkably dull. It moved rather slowly, climaxing in geometry, algebra, and trigonometry in the latter three years. The teaching of analytical geometry and calculus at the high school level was still a thing of the future. I believe my favorite topic was history, partly because of the personality of the two major teachers: Mr. Martin, who had what appeared to be an encyclopedic knowledge of the

United States, and Mr. Jerow, who had a romantic affection for "the glory that was Greece and the grandeur that was Rome." My continuing interest in history I attribute to this early introduction.

A major portion of time and effort was devoted to languages, which for me meant Latin, French, and English. Certainly we all learned to read, and I believe most of us learned to write passably well. An enormous amount of time was devoted to such matters as irregular verbs, both French and Latin, and how to tell a gerund from a gerundive or a subjunctive from a conditional mood. Eventually in both English and Latin studies we got to literature. Caesar's Gallic Wars were followed by the Orations of Cicero and the Aeneid of Virgil. Whereas in French I am certain that we must have read something, what I recall of this instruction is mostly vocabulary lists, irregular verbs, and something called French prose, by which is meant translating simple English sentences into the French language. None of this sparked my imagination. The English courses, particularly those conducted by Mr. Blake, a dramatic and flamboyant teacher, included extensive readings from Chaucer, Shakespeare, Walter Scott, Tennyson, and Dickens.

Laboratory courses in chemistry and in physics were taught by Mr. Bruce and Mr. Payne. These were clearly my favorite subjects, and I apparently excelled since I was awarded a medal in science upon graduation. This laboratory exposure was certainly of some importance in my later selection of subjects when at college. Mr. Payne was a gentle person who also served as the scout master of the Boy Scout troop. Mr. Bruce, a cheerful Scotsman, punctuated the laboratory exercises with his shout of "Make way for liberty!" as he carried heavy carboys of reagents from one desk to another. Curiously, I do not recall any course in biology at this period of my life.

The education that was provided to us by the Horace Mann School for Boys certainly accomplished its chief objective. It got us all into the colleges of our choice. The school had a standing relationship with the admissions office of Harvard College, whereby those students graduating in the upper seventh of the senior class were automatically and without examination admissible to Harvard. Of our class of approximately 50 students, 6 of the successful 7 actually did go to Harvard in 1926. We all found that academically we had been well prepared for the course offerings at Harvard, although by today's standards we were all of us woefully immature socially. During our

high school years, there was little time or energy left over for such frivolous matters as girls. Schooling had been a serious business.

During all of these years, my parents had developed the firm custom of going to Europe every summer. There was an excellent justification for this form of vacation. Where in earlier years the family had withdrawn from New York to resort areas in Maine or upper New York state, this proved unsatisfactory to my father. With his growing surgical practice, he felt that as long as he was within telephone communication of New York, his patients could summon him back to the city whenever they felt they needed his services. It must be recalled that, at that time, travel to Europe was exclusively by boat and each passage consumed from 5 to 7 days. Furthermore, use of transatlantic telephone service was beyond most people's imaginings. Therefore, if a surgeon fled to Europe, he was more or less assured that he would not be summoned back to his examining room or operating room at the whim of a patient. For two summers my parents placed Margaret and me in summer camps and went to Europe without us. This, however, did not work out too well. Neither Margaret nor I particularly enjoyed the camper's life; and my mother, who was by disposition a worrier, could not fully enjoy her European tours. I spent the summer of 1919 in a small camp run by a violin teacher, Mr. Mittell, on a charming lake in the wilderness of New Brunswick, Canada, and a second summer in a more commercial boys' camp on Lake Kennebec. Here I was exposed to a small dose of hunting, trapping, fishing, canoeing, swimming, and natural history. I truly did not enjoy these exposures very much and have only limited recall of what happened. In subsequent summers, Margaret and I traveled with our parents.

The trips would always start with a sailing from New York, first upon ships from the Hamburg-American Line, subsequently on those of the Italian Line. A first-class crossing on a major ocean liner in those days was an extraordinary experience. The accommodations were sumptuous, the boats were immaculately kept, the opportunities for exploring were great, and the food and service were remarkable, both in quality and in quantity. Our father was quite a gourmet and we all followed the course which he set. At each meal one was offered a long list of mouth-watering items on the menu from which one might select as many items as one desired. There were three formal meals each day in the dining room and, in addition, bouillon on the deck every morning, tea with cakes every afternoon, and an evening snack in the bar. Such delicacies

as caviar, foie gras, and clear turtle soup were frequently offered and frequently indulged in. Available entertainments included shuffleboard and deck tennis on the boat deck, swimming in the pool, and dancing to a live orchestra both afternoons and evenings. In addition, there was a movie every night; and once on each crossing, usually after the "captain's dinner," a show was put on by the passengers in which I sometimes participated with a few magic tricks. On various occasions I shared billings with Charles Evans Hughes, Beniamino Gigli, Giovanni Martinelli, and Richard Rogers. Every evening for dinner we would, of course, dress and this for me meant a tuxedo, complete with black bow tie and a boiled shirt. After dinner, in the smoking room, there would occur a peculiar gambling event in which passengers were given the opportunity to bid for the possession of numbers covering the range of expected nautical miles in the next day's run. Thus, if the expected run was of the order of 500 miles, the numbers 490-509 would be placed at auction and lively bidding would ensue. Then, in addition, the low pool, that is all numbers below 490, and high pool, all numbers above 509, would also be auctioned off. On the following noon the officers of the bridge would announce the official day's run, and one of the participants would capture the entire pool, with the exception of 10 percent which was distributed among the smoking room stewards. It was quite extraordinary to see the warmth and fervor which this foolish game engendered among the passengers.

Other gambling activities included lively games of cards in the smoking room, with often considerable quantities of money exposed on the table. I assume that the rolling of the ship made roulette an improbable activity. However, the gambling instinct is not to be denied. There were, each afternoon, hotly competed horse races on the deck in which six wooden horses, each painted a different color, would proceed stepwise as dictated by a set of dice rolled by the chief steward. Both parimutuel betting and side wagers were tolerated. I learned to accept these activities though I must admit I was never particularly tempted to participate.

On each crossing there were conducted tours to the captain's bridge and to the engine room, which I always attended. I was particularly interested in the radio shack. Radio was still a relatively young activity and equipment by present standards was remarkably simple. It had been a hobby of mine since approximately 1920, when I built my first radio set, following instructions in the journal QST, the official publication of the American Radio Relay League.

This organization had been founded by a Connecticut inventor, Hiram Percy Maxim, who was reputed to be the son of the inventor of the Maxim silencer. The ARRL, which had a membership of many amateur radio operators, was able to assemble relay channels and get messages back and forth across the country by passing them from one station to another. The range of each individual station in those days was fairly limited. Actually I never secured a license, so I never had a transmitting station. I did, however, build my first receiver which depended upon a galena crystal as a detector and was tuned by a tuning coil which I wrapped around a wooden rolling pin. All the necessary parts were carefully selected from the stock of fascinating goods displayed by my friends, the Brunner Brothers, at their corner store. Armed with this equipment and a set of headphones purchased out of carefully hoarded allowance money, I listened to the conversation of local amateurs, much of it in code. Only one friend of mine, an upper classman at the Horace Mann School named Arthur Gutterman, had a radio receiving set. But his set, in contrast to mine, was a commercial job. It was with him that I listened to what was the first radio broadcast in the United States. It originated from station KDKA in Pittsburgh, Pennsylvania, and it carried the voice of the great soprano, Madame Tetrazzini, singing Italian arias for the benefit of the sailors of the American Navy then at sea. This event occurred in 1920 when I was 11 years old. From that time forward I was bitten by the bug and constructed, one after another, a series of radio receiving sets of increasing complexity.

During the years of our involvement in World War I, 1917-1918, radio tubes were not on the market. The entire output was made available to the ships of the United States Navy. Shortly after the conclusion of the war, however, this new miracle--the discovery of Lee DeForest--hit the public. I recall very well my initial purchase of one Audiotron (detector) and two Radiotrons (amplifiers). These were costly treasures valued at about \$7 each. The Audiotron contained two filaments, thus doubling the normal life of the tube. It was not equipped with a base but rather had pigtails which had to be connected directly into the circuitry. All filaments were rated at 6 volts and were driven by an automobile storage battery which required frequent recharging. My ultimate set was a superheterodyne built from designs by Armstrong, one of the leading innovators in radio circuitry. Its power was such that I could create enough sound by placing a megaphone against one of the earpieces of my headset to supply music to the entire room. Loudspeakers

at that time were, for my limited funds, prohibitively expensive. The antenna on the roof was approximately 50 feet long and entered my room through an impressive lead-in insulator, equipped, of course, with a lightning arrestor. These were considered essential features to every well-equipped radio station at that time. In order to recoup my investment, I finally sold this set, now boxed in a handsome wooden cabinet, to my uncle, Morris Ernst, who wanted to be the first man on his block to have a radio set of his own.

I have continued to have an interest in electronics throughout my life. This served me in good stead when later on I became a biochemist. I was able to participate with my friend, Fred Rosebury, in probably the second glass electrode in the world for the measurement of pH. This instrument, which had been designed by Dole and MacInnes at the Rockefeller Institute, had to be duplicated at P & S. The high internal resistance of the glass electrode imposed stringent conditions upon the design and construction of the required DC amplifier and taxed the limits of the then available electronic technology. I also took a hand in the construction of two mass spectrometers, one at Columbia and another at the Public Health Research Institute some years later.

Returning now to our European summer tours, travel in the early 1920s in Europe was quite different from what it is today. Mostly we traveled by chauffeur-driven rental car. One summer, for instance, was spent entirely in England and Scotland where, to the amazement of the natives, we managed to travel some 8,000 miles completing a large figure 8 tour. We saw innumerable cathedrals of perpendicular Gothic. We visited the tombs of many kings and poets. We admired the Roman ruins at Bath and the monuments at Stonehenge. We also consumed many meals featuring such delicacies as boiled vegetable marrow, a sort of gelatinous boiled cucumber, usually contaminated with sand, and gooseberry tart topped with Bird's custard sauce. In the family we soon came to call this "semi-detached gooseberry tart," because the stewed gooseberries and the crust apparently met each other for the first time on the plate on which they were served. In general, food on this British tour was undistinguished. I do recall, however, one remarkable exception, and this was in the fairly dreary manufacturing town of Newcastle-upon-Tyne. Here we pulled up at a small inn, tired and hungry. When we entered the dining room the headwaiter asked us what we would like, and my father by way of jest said, "How about some caviar?" The headwaiter immediately responded in the

affirmative and soon returned with a small wooden barrel packed to the brim with large fresh caviar. It appeared that Newcastle-upon-Tyne was the port of entry of all caviar to the British Isles. After serving us generously the headwaiter, who by now had sized up these insane American tourists, told us that the grouse season did not open for a few days but a friend of his had, by accident, shot a couple of birds yesterday and he might be able to serve them to us. We assented with enthusiasm and thus dined in high style in a most unpromising town. Other summers were spent in other countries. One year we toured the chateaux of the Loire Valley. Another took us through the Rhineland and some of the German university cities. Our favored travel, however, was in Italy, and here we finally worked out what became almost a routine.

The Italian line provided excellent modestly sized liners and a pleasant crossing to Naples. Here we would always stop at the Excelsior Hotel where we soon became intimate with its concierge, Mr. Izzo. The concierge of a major European hotel was in those days a person of vast importance. He welcomed the guests, he selected their rooms, and he provided them with all of the many services which they might need. Mr. Izzo, as a sideline, operated a car rental service and thus it came to pass that summer after summer we would rent a grey Hispano-Suiza which, it was rumored, had once been the personal property of the Crown Prince of Italy, Umberto. This car was always driven by a charming and handsome, relatively young Italian named Amadeo who, so my sister averred, had gorgeous dark eyes. He spoke but little English and none of us were fluent in Italian, but this did not seem to make much difference. My father was an aficionado of road maps and an avid reader of Baedeker's guide books. These precious little red-bound volumes, printed on thin India paper, were invaluable compendia of all kinds of information which a tourist might wish to know. Consequently our tours were quite organized, and there cannot have been many churches, museums, fountains, monuments, or other sites that we missed. We saw it all. As the youngest member of the family, it was my job to carry the massive and heavy Graflex camera, which my father favored, as well as a cumbersome and costly set of Zeiss binoculars.

Nor were the gastronomic aspects of touring neglected. Thus we savored the mutton at Simpson's in London, the pressed duck at Le Tour d'Argent in Paris, and fettucini at Alfredo's in Rome. All of us would gain weight on these European tours--particularly my sister and my father. In consequence of this we would sometimes include a Kur in our tour. I recall, for instance, a

couple of weeks which we spent at Baden-Baden. Here my family all checked in at the sanitorium of Dr. Dengler, situated up in the hills behind the town. Since there was nothing in particular wrong with me, I was put up at a splendid hotel, The Stephanie. After a while, however, my parents decided that it would be wiser and safer if I also took the Kur. I well recall my interview with the formidable Dr. Dengler who asked me what was the matter with me. When I told him that I felt fine, he said reassuringly, "Don't worry, we will cure you." He then prescribed for me the following ritual. Each morning at 6 o'clock a muscular German lad would come in and give me a vigorous and unpleasant massage with ice cold Brandtwein. Then I would be required to dress and walk the mountain trails, up hill and down dale, for half an hour. After that we were ushered into the dining room where we were each fed a diet carefully controlled by having our room numbers imprinted on each dish and cup. Then we would sit in the foyer waiting to be summoned to the baths. My own personal cure involved lying motionless in a tub for a long period of time while the tub was filled with warm carbonic acid. As the bubbles of carbon dioxide accumulated on my skin, I would become progressively hotter. After a period of time I would be allowed to take a cold shower. On alternate days I would be placed in the middle of a tiled room which had a stanchion that I soon learned to clutch with all my strength. Then a sadistic young man would pick up a fire hose and squirt me at high pressure with water, the temperature of which rapidly oscillated between very hot and very cold. After a scanty lunch we were again required to walk up in the hills. Many of the guests at Dr. Dengler's took this occasion to visit the pastry shops in the beautifully laid out gardens of the city, thus offsetting many of the benefits of the treatment. After a while my family had taken as much as they could of this Spartan living and we again hit the highways.

Thus, over the years, I saw the principal tourist attractions of England and Scotland, France, Holland, Germany, Austria, Italy, and Switzerland, as well as parts of Spain and Yugoslavia. I exhausted my appetite for touring and sightseeing and today I travel reluctantly. I have seen the principal paintings of the Prado, the Uffizi, and the Louvre. I have counted the stained glass windows at the Cathedral of York and have admired the mummy of San Carlo Borromeo in the crypt of the Cathedral in Milano. I have watched the horse guard at Buckingham Palace and have kissed the lapis lazuli ring of the Pope, carefully holding it at a modest distance from my lips under

instruction from my surgically trained father. I have traveled by gondola and funicular. However, largely because of all of these activities, I never did find occasion to learn to ride a bicycle or to roller skate. I swim but poorly, have played little tennis, and no golf in my life.

Memorable was the summer of 1924 when I was dispatched to Europe in the company of John Mulholland, my teacher in manual training and in magic. On this occasion we confined our trip to the British Isles--England, Scotland, Ireland, and Wales. We visited virtually every magic store and we met with many magicians. I particularly remember the emporium in London of Will Goldston, who was the private instructor in magic to the then Prince of Wales. He took us as guests to the Magic Circle, a club of amateur and professional magicians in London, where we showed each other tricks for our entertainment and instruction. On that particular evening his Royal Highness did not show up. I also recall many visits to the music hall operated by two famous magicians, David Devant and Neville Maskelyne, called St. George's Hall. This curious little vaudeville theatre was almost totally dedicated to magic. Except for an occasional juggler, all of the performing artists did tricks. The featured performers were, of course, Devant and Maskelyne. I know of no comparable theatrical production anywhere in the world. Unfortunately, St. George's Hall was destroyed during World War II and magic has certainly declined as an entertainment form. I vividly recall David Devant performing his featured disappearing birdcage, an illusion which had been introduced by an earlier French magician named de Kolta. Devant would walk on the stage holding a small birdcage containing a live canary. Then suddenly, with a broad smile on his face, he would appear to throw the birdcage into the audience and lo and behold it disappeared. I can attest from personal experience that this is a difficult trick to do. I purchased such a cage, inserted into it a fake canary, and practiced many, many times. I could never achieve the elegance of Devant's performance and never included this trick in my regular shows.

On my return to the United States I joined the Society of American Magicians as their youngest member. I was intrigued by the emblem of that Society--two serpents each devouring the other's tail. Houdini was at that time its president. He was a muscular and aggressive man whose life was largely run by his small, fragile wife, Beatrice. Frequently attending the monthly meetings at the Hotel McAlpine were Howard Thurston, Harry Blackstone,

and others of magical preeminence. Short business meetings were followed by fascinating exhibitions of tricks. On a later visit to London I dropped in on Will Goldston, who invited me to a meeting of the Magic Circle of London. When I arrived at the meeting place, I learned from others that the featured entertainment that evening was to be a young visitor from America. It wasn't until after the supper that I learned that I was it. Fortunately I had in my pocket a beautifully manufactured "shell" of an American half dollar, the like of which was totally unknown in England, and with this I had the pleasure of bewildering the cream of British magicians.

Back in New York, our family had prospered and we finally left the comfortable brownstone house on the West Side and moved into a more elegant apartment house on Park Avenue at 77th Street. This address was convenient because it was directly across the Avenue from the Lenox Hill Hospital where my father spent most of his time. On the ground floor of the building he had his offices, while our residence was on the sixth floor. My commutation to high school now included a trip across town from Park Avenue to Broadway in the morning and the reverse in the evening. I never truly adapted to the Park Avenue address and several years later I progressed to Harvard College. In 1926 I graduated from the Horace Mann School for Boys with honors in science. A considerable group of my classmates and I then took advantage of the Harvard admissions process and moved to Cambridge.

I recall that, returning from Europe in the summer of 1926, I became ill, contracting what would be called hepatitis today. Deeply jaundiced, I was admitted to Lenox Hill Hospital on the service of Dr. Max Einhorn, its chief gastroenterologist, who had invented a torture device called the Einhorn bucket. This was a large gold lozenge at the end of a long rubber tube which the victim was required to swallow. The bucket was allowed to proceed through the stomach into the upper intestine where, in my case, it was kept for a period of about one week. During that time my duodenum was thoroughly washed through the tube with a continuous infusion of magnesium sulfate solution which was supposed, in those primitive times, to stimulate the secretion of bile. Perhaps it truly did, because at the end of a week I was discharged from the hospital and proceeded somewhat belatedly to join my schoolmates as a freshman at Harvard College.

Chapter III

FAIR HARVARD

In September of 1926 I took up residence in suite B24, Gore Hall, then one of the freshman dormitories of Harvard College. Gore Hall was a fine modern Georgian-style building fronting on the Charles River. Since that time it has been incorporated into the Harvard House Plan but that transformation occurred shortly after my graduation. Our suite had four small separate bedrooms, a well-sized living room, and a bath. We were a group of Horace Mann boys-- Jerry Frank, Alan Brown, John Chandler, and myself. John Chandler and I have had little contact since college days but I continue to see Alan Brown and his charming wife Beatrice from time to time. After earning a doctoral degree in literature at Columbia University, he served as president of Hobart and William Smith Colleges and is now emeritus professor of English at the Mayaguez campus of the University of Puerto Rico. Living immediately next door was classmate Lincoln Kirstein, later famous as a leading figure in the American ballet. Eliot Cook Carter, who also moved with us from Horace Mann to Harvard, majored in music and became one of America's leading serious composers. Another among my classmates was Edwin Land, who during his early college years invented the sheet polarizing material for which he later became famous. I well remember his showing us small fragments of a pale purple transparent plastic material which polarized the plane of transmitted light so that when two pieces were rotated, one with respect to the other, there was alternate transmission and non-transmission of light. At that time the major application that Ed visualized for this startling discovery was the incorporation of the material into the headlight lenses and windshields of cars to reduce glare from oncoming vehicles. He was unsuccessful in securing the needed legislation to make this application universal. He subsequently dropped out of college to found the Polaroid Corporation.

Gore Hall was equipped with an elegant commons room and dining hall for its students. We had as resident proctor a graduate student who was scion of the family which owned the famous toy store in New York, F.A.O. Schwarz. The accommodations by any standards were sumptuous and we managed to make ourselves quite comfortable. Very early on we were given copies of a little

booklet called Parietal Regulations. I recall that among the rules of conduct included in this volume were the absolute exclusion of all women from the dormitory after sundown and an enjoiner against the discharge of firearms. Also, since these were the days of the Prohibition Amendment and the Volstead Act, liquor was forbidden on the premises. I may say that we took these rules quite seriously. We were, it appears, of a docile generation. We soon adapted to the simple, relatively monastic life of Harvard undergraduates. It was my habit to mail home every week or two a fiberboard box full of soiled laundry and await eagerly the return of this box, now filled with clean linen and such goodies as my mother might see fit to include. This was also Jerry Frank's practice. The Frank family, at that time, had a domestic whose specialty was a peculiarly delicious confection called Linzer Torte, made largely of ground nuts and raspberry jam. The arrival of such a delicacy would signal the occasion for a party. For the rest, except for occasional expeditions to the movies or a Saturday football game, we spent most of our time studying. We had been thoroughly habituated to this life by our experience in high school.

Elementary chemistry was taught at that time by a Dr. Hall in a building, Boylston Hall, which was peculiarly poorly adapted for laboratory work. Dr. Hall, I remember, was a distinguished inorganic chemist and a follower of Harvard's only Nobel laureate of the time, Theodore Richards, who had developed and perfected exquisite methods for the precise estimation of atomic weights. Richards and his students had noted that samples of lead derived from various sources had slightly differing atomic weights, and this was correctly attributed to the fact that lead is a mixture of several isotopic modifications. To Dr. Hall was given the assignment of trying to separate the isotopes of lead by fractional crystallization of one of its salts. It was common rumor that he had recrystallized samples of lead nitrate hundreds--or perhaps thousands--of times. Whether he actually demonstrated significant separation of isotopes I do not recall. However, in the course of these experiments he apparently did acquire some level of lead poisoning, with resultant total loss of hair. I remember him as a serious and lucid instructor. Far more interesting in those early years were the lectures and readings of Bliss Perry, professor of English. Perry was an elegant lecturer, a personal friend of most of the contemporary figures on the literary horizon, and a former editor of the Atlantic Monthly magazine. His lectures were lively

and attracted a good deal of attention. In those happy days, whenever a member of the Harvard faculty was about to deliver a particularly interesting lecture, an announcement of this event would appear in the daily newspaper, the Harvard Crimson, and the public at large would be invited. Harvard abounded in great lecturers and Bliss Perry was among the top. I still recall with pleasure his readings extending chronologically from Geoffrey Chaucer to Rudyard Kipling, and my fondness for both of these poets stems from this exposure. He also introduced me in a serious way to Byron, who remains today my favorite poet. Bliss Perry's life exemplified Chaucer's description of the clerk, ". . . and gladly did he learn, and gladly teach." Perry used the last three words of the above quotation to entitle his autobiography.

The president of Harvard at this time was A. Lawrence Lowell, a very dignified gentleman, a former teacher of political science, and a brother of the eccentric cigar-smoking poet, Amy Lowell, and of the astronomer and discoverer of Pluto, Percival Lowell. He was something of an educational innovator and clearly an admirer of the great British universities. It was he who instituted the tutorial system wherein each student was assigned to one or another faculty member for a period of years. The student would consult and commune with his tutor, often on a weekly basis, to discuss his curricular and extra-curricular activities. My initial field or major was biology and I was assigned to Dr. E. S. Castle, an instructor in that department. He was an intelligent young man, brother of William Castle, the great physician at the Boston City Hospital, who was later to achieve world fame for his contributions to the understanding of pernicious anemia. In my junior year I transferred from biology to the young department of biochemical sciences and was then assigned by good chance to Dr. Frank Fremont-Smith, who was at the time a neuropathologist with laboratories at the Boston City Hospital. My association with Frank, which started in 1928, continued until his death only a few years ago. He was himself a graduate of Harvard Medical School, who had matured in the great tradition of neurology at the Massachusetts General Hospital and the Boston City Hospital. His chief was Dr. Stanley Cobb, a world renowned neurologist with a deep interest in the cerebrospinal fluid. It seemed only natural that this should be the subject of Frank's major medical interest at that time. Frank had an active research laboratory which was dominated by a loyal technical assistant, Mary Elizabeth Daley, a remarkably skillful and competent analytical chemist. It was a provision of the tutorial

plan at Harvard that if one entered into an honors program, one might spend a portion of the senior year conducting research under the preceptorship of his tutor, and this I elected to do. As a result, I spent a considerable amount of time in the laboratories of the Boston City Hospital during my senior year and actually completed a small study which constituted my first publication. This study was concerned chiefly with the mechanism of water diuresis and an attempt to construct a simple model to account for the range of variation in the observed concentration of ingredients in the urine. I served as guinea pig, as analyst, and as recorder for these studies which were presented in my honors dissertation, entitled The Constancy of the Internal Environment.

I vividly recall my first encounter with Frank Fremont-Smith. It was early in my junior year that I climbed the four or five flights of stairs leading to the offices of the division of biochemical sciences in Holyoke House on Massachusetts Avenue. This was long before the construction of the present Holyoke Center on the same site. I am certain that I was nervous at the prospect of meeting my new tutor, and I subsequently learned that he was similarly under tension at the prospect of meeting a new tutee. He initiated our discussion by asking me what I had done during the preceding summer, and then, by the grace of God, a fire engine with much accompanying clanging of bells and blowing of sirens came down Massachusetts Avenue. Frank turned to me and asked how I liked fires. I allowed that I could take them or leave them. He, however, was a devotee of fires and firefighting equipment. He therefore suggested that we rush downstairs, get into his small Ford coupe, and chase the fire engine across Cambridge. This we did at peril of our lives and finally came to the site of the fire--which proved to be more smoke than fire. The problem was that the smoke was at the top floor of a 4-story building and there appeared to be no obvious way of getting the hose up to the roof. I recall Frank trying to explain to the fire captain that by sending a fireman up to the roof with a hank of rope, it might be possible to lower the rope to the ground, tie the end to the nozzle, and hoist the hose up to the roof. I do remember that the fire captain dismissed this notion rather abruptly.

Frank was married at that time to a daughter of a former Harvard president, Charles W. Eliot. He had a number of blonde sons and it soon became one of my functions to join his family for supper and entertain the boys with magic tricks.

Frank had a fine inquisitive mind relatively uncluttered by scholarship. He eventually left Cambridge, neuropathology, and Harvard to become medical director of the Josiah Macy, Jr., Foundation. In this capacity he provided for me my first independent research support. He also established an important series of multidisciplinary meetings in various aspects of medical science. Over the years I attended many of these meetings, which under his delicate hand were most stimulating and provocative. He would frequently open such a meeting by enlisting active participation from the attendees with the line: "As the small boy said, 'Don't speak when I'm interrupting!'" No question was too trivial for his inquiry. A man inclined to plumpness in middle life, he had a great fondness for ice cream. I recall very well his calling me one day to tell me that he had just discovered that to eat ice cream must result in loss of body weight. The argument went as follows: To warm a quart of ice cream from the freeze point to body temperature consumed more calories than were derived from the combustion of the nutrients in the ice cream. The numbers which he supplied in support of his argument appeared to be convincing until I had to point out to him that there were two kinds of calories--small calories and kilo calories, one used in physical and the other in nutritional calculations. If appropriate adjustments were made, there was no doubt that the ingestion of ice cream could only lead to an increase in body weight. Frank survived this crushing blow with remarkable fortitude. Through my associations with Frank and attendance at the Macy Foundation meetings, I came to know two of my favorite people: Cecil Watson, long-time professor of medicine at the University of Minnesota, and Charles Best of Toronto, co-discoverer of insulin.

Over the two years of time which I spent as a tutee of Frank Fremont-Smith, I formulated my further educational plans. It was on his insistence that I attended medical school, even though I had already decided that I wanted to devote my working career to the conduct of research. Frank felt strongly that in his own case, and presumably in mine, an exposure to medicine was of great importance in the selection of problems which merited research attention. In retrospect, I have some doubts as to the wisdom of the investment in time that I made in medical school and internship-residency. It was all of value, but it could well be that the time might more profitably have been invested in preparation for a career in research. Research is a young man's game and I got there later than I might otherwise have.

The Harvard faculty abounded in "characters." Most of the freshman class took History I. This course reviewed the history of Europe from the early Renaissance to the present time. The lectures were given by a single professor, Roger Merriman, a large man who wrestled throughout the lecture with an exceptionally long pointer which he occasionally used to direct our attention to one or another feature of a lantern slide. Lectures were given in what was Harvard's largest lecture room, Lowell Lecture Hall. Merriman, I remember, was particularly interested in the history of Spain and the Spanish-speaking nations. His lectures reached a dramatic climax with his description of the Spanish Armada. After disposing of Mary Tudor, Elizabeth, Philip II, Francis Drake, and all of the others, he finally would come to the strategy and the battle plan. Then from the podium came the unforgettable line: "The sea groaned beneath the weight of the Spanish ships." This figure of speech caught my fancy. It was many, many years later that I read a current account of the Spanish Armada and was startled to find this very line, without attribution, in the contemporary historian's account. I was pleased and somewhat relieved to find that this author acknowledged that he had studied under the preceptorship of my old teacher of history.

During my student days, the Harvard Chemistry Department took occupancy of its brand new Mallinckrodt Hall, a combination of teaching laboratories, lecture rooms, and library contributed by the St. Louis industrialist who had been himself a Harvard student. As with every new chemistry laboratory building, troubles were encountered at the time of occupancy. The building was equipped with a central distilled water system piped through very costly tubes of block tin, regarded at that time as the most desirable material for the purpose. The still was situated under the cupola which decorated the gabled roof of this traditional Georgian building. Upon testing, it was found that the distilled water was heavily contaminated, and the contamination persisted throughout the first many months. Finally, it was determined to open the still pot in order to cleanse it, and to everyone's dismay it was discovered that a workman had inadvertently dropped the butt of an old cigar into the bottom of the distillation vessel. With this source of pollution removed, the distribution of pure water was finally established.

The up-and-coming young organic chemist at Harvard at that time was James Bryant Conant. He taught the elementary course in organic chemistry with vigor and briskness. We, the students, had the impression that he was always

in a great hurry, and not infrequently he arrived at the lecture podium carrying a suitcase as though about to leave on an important mission. He had composed the elementary textbook which we used and was a very incisive and clear lecturer, although he seemed to be a somewhat chill and formidable person. He had sometime before married the daughter of Harvard's Nobel Prize-winning chemist, Theodore Richards, and was devoting his own research efforts to studies on the structure of chlorophyll. Some years after our graduation this same James Bryant Conant became, of course, president of Harvard and then, after World War II, high commissioner of Germany. He was obviously a man of considerable wit, as many later anecdotes prove, but as a pedagogue he gave little evidence of humor. I came to know quite well two graduate students in the department, both of whom spent time working with and for Conant. The first of these was Bill Mydans, the son of a musician and older brother of Carl Mydans, who became a renowned photographer of the old Life magazine. Bill and I spent a good deal of time together. Upon completion of his own studies and a short term of service for Conant, he entered upon a career of private industrial consulting, and then, with the outbreak of war, he joined the Chemical Warfare Service. He ended the war with the Army of Occupation in Italy and an assignment to reactivate the Italian chemical industry, a task which he undertook with skill and success. Upon my graduation from Harvard, Bill presented me with one of the most cherished and frequently consulted volumes in my library--History of Medicine by Fielding H. Garrison.

A second graduate student in the Department of Chemistry with whom I had an enduring friendship was Max Tishler. Max, like Bill, was Boston bred, a graduate of Tufts College of Pharmacy, and a registered pharmacist. He determined to better his station in life and earned a Ph.D. at Harvard under the formidable senior professor, Elmer Peter (King) Kohler. Max also served an apprenticeship under Conant and then moved on to the pharmaceutical firm of Merck, where he rose through the ranks, ultimately to become vice president for research. Max was perhaps the hardest working man I have ever known. He labored in the laboratory and in his office for very long hours all his life. Many years later, when I moved to Rutgers University in New Jersey, I reestablished contact with Max and he was very helpful and supportive in my efforts to establish a medical school in New Brunswick. In later life he resigned from Merck and assumed a career as a teacher of chemistry at Wesleyan College in Connecticut, thus fulfilling a life-long ambition to participate in

the teaching process. Max is a serious and interesting man, a deep scholar, and a cultivator of exotic plants. I have relished my contacts with him over the many years.

Organic chemistry in the United States traces its roots to Ira Remsen, who established his school in the Chemistry Department of the Johns Hopkins University. He made many contributions, the best advertised of which was his discovery of saccharin. In addition, he trained many of the next generation of chemists, and among these was Elmer Peter Kohler who led organic chemistry at Harvard College for many years. He was a very sound and productive organic chemist in the laboratory and, in addition, was perhaps the most polished teacher under whom I ever studied. His lectures were truly works of art. He would walk into the lecture room precisely at 7 minutes after the hour and, without notes or lantern slides, commence his lecture always with the opening line, "We were talking last time about" His lecture would terminate in exact synchrony with the great bell on the clock in Memorial Hall which could easily be heard in the lecture room in the Mallinckrodt Building. It was pointed out that 53 minutes, the traditional length of a Harvard lecture, was precisely one microcentury. He was particularly concerned with mechanisms of organic chemical reactions and this was the subject of his famous course, Chemistry V. Clearly his favorite organic substance was benzalacetophenone, and with this as model he was able to demonstrate a host of chemical phenomena. Organic chemists at that time almost invariably represented the valence bond between two atoms by one or more dashes. Thus between two carbon atoms one might draw one, two, or three dashes, depending upon the structure and the substance. Kohler was one of the first to appreciate the advantages of replacing each dash by two dots representing the shared pair of electrons that were involved in each covalent bond. This transition through which I lived as a student was sometimes referred to as the conflict between the dot and the dash chemists. Chemistry V was the course which separated the men from the boys and was at the time and for many years after correctly appraised as a difficult course. In his personal life, Kohler was an inscrutable bachelor whom no one, even his graduate students, came to know intimately. He was strictly business.

Perhaps the most colorful faculty member with whom I had contact was Lawrence J. Henderson. His large head and full reddish beard, together with the tightly buttoned jackets that he affected, gave him the appearance of an

idealized Harvard professor. He was, in fact, a man of great wisdom and scholarship. There were few topics upon which he could not comment productively, whether the history of chess, the practice of pediatrics, or modern economics. The contribution to which his name is permanently attached is the so-called Henderson-Hasselbalch equation. As often turns out to be the case when the origin of a name is traced, it would appear that Henderson's contribution was a modest one. Hasselbalch had earlier established the approximate mathematical relationship between the dissociation constant of a weak acid, the concentration of that acid, the concentration of a salt of that acid, and the resultant hydrogen ion concentration. What Henderson actually did with the Haasselbalch equation was to translate it into logarithmic terms, and it is this form of the "buffer" equation that every medical student must learn by heart.

$$\text{pH} = \text{pK} + \log \frac{\{\text{salt}\}}{\{\text{acid}\}}$$

Henderson, however, made many other important contributions to biological chemistry. He studied extensively the multivariant system of the blood and its simple ionic solutes, particularly as these varied at work and at rest. In order to treat conveniently the immense number of data thus secured, he adapted for the first time in biological sciences a mathematical trick called the d'Ocagne Nomogram, an ingenious method for representing many variables simultaneously on a single piece of paper. This method found extensive use in succeeding years among biologists until it was finally relegated to obscurity by the advent of the computer. Henderson was perhaps the first biologist to appreciate the beauties of the biological system, carbon dioxide-water-bicarbonate ion. This system he extolled in his volume The Fitness of the Environment. I enjoyed L.J. as a teacher in the course in biological chemistry offered at the college and also in a course in the history of science. His laboratory activities were housed in the then new Harvard School of Business Administration, where they were tolerated because of their purported relationship to the efficiency of human work. His blood studies were performed upon fellow faculty members and athletes, including Paavo Nurmi, the perennial winner of the Boston Marathon and affectionately known in Boston as "The Flying Finn." Henderson's study of the composition of human blood from subjects at rest and at work was assembled in his book, Blood, A Study in General Physiology, which is still a cherished book on my shelves. He was the

closest thing to a Renaissance man that I ever met. There was no subject upon which he could not discourse. There were few in which he was not expert. He, together with A. Lawrence Lowell, established the Harvard Society of Fellows, a structure modeled after that in Cambridge, England, to provide a haven for both junior and senior scholars free of almost all responsibilities. Several years later, he discussed with me the possibility of joining this elite group but nothing came of it. Politically he was an arch conservative, and his economics was based upon that expounded by Pareto who, it may be recalled, also gave guidance to Benito Mussolini. In fact, the English translation of Pareto's works was done by L. J. Henderson.

One of my favorites on the Harvard faculty was George Sarton, professor of the history of science. If Henderson was a Renaissance man, Sarton was a medieval monastic. He had commenced his enormous study of the history of science while still in his native Belgium. When, in World War I, the German Army marched into Belgium, Sarton buried his notes in his garden and fled to the United States where the Carnegie Institution provided a position for him at Harvard. After the war he was sent back to Belgium, where fortunately he was able to recover his earlier notes and bring them to Widener Library on the Harvard campus. Building upon these papers, he assembled an enormous amount of information on the history of science which he collected in his module in Widener Library. His appetite was catholic. Since he mistrusted all translations, it became necessary for him to try to master all of the common languages, and it was rumored that he was literate in some 22 of these. He was lured out of the library two or three hours each week to give lectures on his beloved topic, and these were a sheer delight to the relatively small classes that he addressed. History of science was not then, nor is it today, a terribly popular subject among college students. He lectured with authority on many diverse topics such as the history of musical notation, the fabrication and erection of obelisks, or the application of the statistical method to early meteorology. He regarded the domain of science as including all aspects of man's intellectual efforts that are heavily dependent upon a written record, and he was in the process of preparing his enormous compendium, Introduction to the History of Science. This appeared over the years in five blue-bound massive volumes which I avidly acquired. The world of antiquity from Homer to Omar was readily disposed of in a single large volume. Then, however, as has happened to other scholars of history, Sarton got bogged down

in the Middle Ages. He discovered that there was vastly more information about medieval contributors to science than had previously been assumed, and all of this had to be recorded. Succeeding volumes encompassed only one century or one-half century each, and it was clear that the set would never be completed within his lifetime. Therefore, in later life he turned his attention to another set to be called simply A History of Science, and of this he managed to finish two volumes before his death. These covered science through the Hellenistic Era and are, in my judgment, the most readable and informative books covering this piece of history. They are an invaluable source of interesting information. Here one may find, for example, a detailed discussion of the death of Socrates by hemlock poisoning, the descriptions of this event by Plato and Xenophon, and a comparison of the symptoms and signs described by these two observers with contemporary studies of the poisoning due to coniine, the toxic principle of hemlock.

As may be imagined, Sarton's lectures were tightly packaged with enormous quantities of information. He welcomed questions from the students, and the vastness of his knowledge permitted him to provide authoritative answers. I recall that once after a lecture he was asked if the Irish mathematician Hamilton was related to the British Ambassador to Naples of the same name, and he immediately responded giving the precise degree of relationship. He was the founding editor and major contributor to the journal of the history of science, *Isis*. Some years after leaving Harvard I met a Chinese pharmacologist, Kwei Djen Loo, who had been invited by Sarton to contribute an article to *Isis* on the ancient Chinese pharmacy. After he had reviewed her manuscript, he accepted it for publication but told her that she had incorrectly transliterated her name from the Chinese and that he would therefore correct the spelling of her own name at the time of publication. This, as you may imagine, led to a bitter dispute. I do not recall whether the article eventually was or was not published.

There were, of course, numerous diversions, academic and otherwise, available to the undergraduates of Harvard during the period 1926 to 1930. Thus, the Boston Symphony and Arthur Fiedler had just recently spawned the Boston Pops, an informal concert series available at low prices after completion of the formal concert series, and these we often attended. Also, there were lectures and readings available to all. One of the odd figures who lived on the Harvard campus was Professor Charles Townsend Copeland, a student of

English literature, who believed in the dying art of reading aloud. From time to time he would hold readings, generally in the big hall of the Harvard Union, an eating and recreation institution designed to provide a social outlet for the majority of Harvard students who did not belong to one or another fraternity or club. Here Copey, as he was affectionately called, would mount the podium with a large stack of books, each bearing one or more bookmarks, and from these he would read. He favored the English poets and he read remarkably well. He could easily hold a group of several hundred Harvard undergraduates spellbound for a couple of hours after supper. Copeland readings became a fixed institution at Harvard, and before his death he published a large volume of his favorite works for reading aloud. It is to be regretted that with the advent of the noisy media, radio and television, the art of reading aloud has almost entirely disappeared. Then, of course, there were the movies. It was during my undergraduate years that the first "talking pictures," led by Al Jolson in "The Jazz Singer," made their appearance, and there was a movie theatre conveniently located at Harvard Square. Occasionally we would venture into Boston where the new and splendid Metropolitan Theatre would present feature pictures and other stage entertainment. It was here that I first heard the great Paul Whiteman Band, and I vividly remember a presentation introducing a quartet called "The Harmony Boys," featuring an unknown young singer named Bing Crosby and a song called "Mississippi Mud." Many years later, shortly before Whiteman's death, I met the retired band-leader at a social gathering in New Jersey and reminisced with him about his association with Bing Crosby. He commented: "I should have stuck with that young man."

I also continued to pursue my own hobby of magic. I covered every magician who came to town, including the great three of that era--Houdini, Thurston, and Blackstone. I would not only witness their performances but would, on occasion, meet them in the back room of Sam Bailey's magic emporium, located on the second floor of an office building at Central Square, one stop away from Harvard Square on the subway line. I spent many pleasant Saturday afternoons in that fascinating shop with its fascinating proprietor. Sam Bailey, a diminutive man with a monumental wife, had been in magic one way or another all of his life. As a younger man he ran a medicine show, traveling by horsedrawn cart through the New England villages and selling various proprietaries. He told me that his best item, which sold at \$1 per bottle, was his old

Indian corn cure. He would ask if anyone in the audience was at that moment suffering from the pain of corns. Inevitably a farmer would come out of the audience admitting to such discomfort, and almost always he would be wearing a pair of stiff heavy leather boots. Sam would explain that his corn cure was so powerful that it actually worked right through the boot, and he would pour the contents of a bottle onto the farmer's shoe. The bottle, which contained turpentine and nothing else, would soften the stiff leather and immediately the farmer would find great relief and would show his pleasure. After that, Sam would sell as many bottles as he could and then get out of town before the inhabitants discovered what they had actually bought. His magic store was a highly sophisticated place where chiefly professional magicians convened. During my early years at Harvard I perfected my own magic act, which included such tricks as Houdini's needle-threading trick, the linking rings, some handkerchief knot tricks, and the fish bowl production. By my senior year I was ready to join the Harvard instrumental clubs as an entre acte between the performances of the mandolin club and the banjo club. During the Christmas vacation that year, the instrumental clubs went on tour through many larger southern cities. We lived in a chartered railroad sleeping car and put on productions each evening in such cities as Birmingham and Nashville, always followed by dances arranged by the local Harvard Clubs. This was the closest I ever came to a professional stage career.

I have many memories of my years at Harvard. For two years, Jerry Frank and I shared quarters on the third floor of a small dormitory called Drayton Hall. In the suite immediately below us was a friend and classmate, Leonard Wallstein. An accepted practice among Harvard undergraduates was to irritate one's friends by throwing pebbles against the window when the inhabitant was known to be cramming for an examination, thereby distracting him. I recall one evening when Leonard went down in the street and engaged in this pastime against our study window. The accepted defense against this practice was to throw a bucket of water out of the window in the hope of discouraging the miscreant. On this occasion we waited our turn until it was clear that he had returned to his own apartment immediately beneath us. Meanwhile, we had prepared our instrument of revenge. It was a paperweight fastened to the end of a piece of string, which we dangled out of our window and allowed to tap against his. He naturally assumed that we were down in the street, and after a while his window opened and we knew that he must have a pitcher of water in

his hand. We waited until he stuck his head well out of the window and then from directly above him we let him have it with a full bucket of water. It was both a strategic and a moral victory.

In our senior year we moved, as was then the practice, to one of the dormitories on the Harvard Yard, Matthews Hall. Here we had a suite equipped with a beautiful wood-burning fireplace and here we enjoyed all of the perquisites of being Harvard seniors. We were, I am certain, by the standards of more recent generations, remarkably well behaved. Drugs, as far as I was aware, were not used and were not discussed. Even alcohol was rarely encountered since, as will be recalled, the prohibition amendment was then in force. It is true that on rare occasions we did go to one or another speakeasy where we would surreptitiously drink bad red wine out of teacups, always with one eye to the door in the event of a raid. To be caught in such a raid was to risk one's continued attendance at Harvard. Women were essentially excluded from the Harvard dormitories so that socializing was limited to restaurants, theatres, movies, and occasional invitations to one or another home. I had no car at the time, nor did any of my roommates. Indeed, ownership of autos was the unusual rather than the usual practice. We came to know the metropolitan transit system quite well.

In the light of what has happened since, there was a surprising lack of interest in ethnic problems. I recall few students belonging to minority groups in my class. The one big issue of a political sort which enlivened our discussions throughout my four college years was the Sacco-Vanzetti case. For those who have never heard the story, it relates to the arrest of two Italian-born avowed anarchists on the charge of killing a paymaster during a robbery and their subsequent trial in Dedham, Massachusetts. It appeared to much of the undergraduate population that the trial was conducted in a grotesquely unfair way and that the judge conducting the trial was patently biased against the defendants. Studies of the case over the ensuing years still leave in doubt whether Sacco and Vanzetti were, in fact, actually guilty of the shooting. There is little doubt that the trial procedures left much to be desired. Sacco and Vanzetti were ultimately convicted and sentenced to die. Governor Fuller established a blue ribbon committee comprising the presidents of Harvard and MIT and the Bishop of Boston to review the evidence. There ensued a storm at Harvard when Felix Frankfurter, then professor of law at Harvard, seriously criticized A. Lawrence Lowell's review of the case and was

promptly asked to resign by the president of Harvard. As soon as it was known that he had resigned, a majority of the faculty of the law school resigned in sympathy, as did its dean, the renowned Roscoe Pound. President Lowell realized that he was licked and graciously reinstated Frankfurter and the rest of the faculty of the law school. All of these activities had their effect upon an otherwise indifferent student body. There were a few riots in the subway system, and occasional students chained themselves to the fence of the Boston Commons and made impassioned orations against the judiciary and the government of the state. All of this may have relieved the students of some tension but had no impact upon the execution of Sacco and Vanzetti. This occurred during the summer when I was, as usual, traveling in Europe with my family. The day of the execution was a day for anti-American riots in many major cities of Europe. We happened to be that evening in the city of Brussels and were advised by the concierge of our hotel not to go out on the streets. We disregarded this advice and walked in the beautiful main square surrounded by its ancient buildings. A restless crowd had gathered, but the Brussels police department managed the problem with a squadron of mounted police that galloped hither and yon across the square breaking up gatherings of citizens who might otherwise have started to riot. We read the next day that in Paris there had indeed been riots which were quite destructive.

A home that I visited fairly frequently was that of the Jack family where the chief attraction was the pretty daughter, Betty. They lived in a farm house in Walpole which was surrounded by an extensive apple orchard. Here they kept bees which I mostly shunned, and of course apples which I helped to pick. Mr. Jack was a large and muscular man, professor of dendrology at the Harvard Arboretum, and one of the first patients whose pernicious anemia was held in check by the then recently discovered administration of whole liver. Mrs. Jack was a bustling do-gooder who was always organizing Harvard students into one or another project. I recall that she regularly visited the Dedham jail to teach English to Vanzetti. It was at the Jack home that I met Mr. Gill, recently named commissioner of prisons for Massachusetts. He was a reformer, an advocate of indeterminate prison sentences with termination to be decided not by the judge but by the prison staff. He constructed a remarkable prison devoid of locks and bars for which he substituted his remarkable powers of persuasion. He actually succeeded in getting the prisoners to patrol the boundaries of the prison to "exclude the outside population." Each new

prisoner was encouraged to paint his room to his own taste. The resulting contrasts might have shocked interior decorators but this procedure, according to Mr. Gill, afforded the prisoners great satisfaction. An invitation from Mr. Gill to perform magic tricks for his prisoners clearly could not be declined and I spent a delightful evening entertaining the inmates.

One summer during my years at Harvard I spent on the Modesto, California, ranch of my friend Arthur Tomey. I had known Arthur as scout master during my grade school years. He had been a divinity student at Union Theological Seminary but, like many of his classmates, had decided in his later years at that institution not to follow a religious calling. Through our San Francisco friends Herbert and Ethel Walter, my family put Arthur in touch with California farmers who found for him a turkey ranch, and I went out one summer to assist him in his transition. The economy of this particular farm was fairly complex. Alfalfa had to be cultivated in order to nourish a herd of about 20 cows. The cows had to be milked twice a day and the product passed through a cream separator. The cream was then sold to the local dairy cooperative which transformed it into butter, while the skimmed milk was reserved to feed to the turkeys. A flock of about 1,000 turkeys was fattened in order to get it to market in time for Thanksgiving when turkey prices were maximal. Arthur had, in addition, a small peach orchard on an irrigated piece of land. I recall that we got the irrigation water for about 4 hours each 18th day. This was a period of furious activity, opening and closing of flood gates, and directing the water into the orchard. The orchard was surrounded by a very modest earthen dike, but during the 18-day interval it would have been perforated by rodents. It therefore was necessary to rush around the field with a shovel, patching up the perforations in order to retain the water. Within the next few days the ripe fruit had to be picked in order to get maximal advantage of the irrigation process.

We lived modestly but fairly well on Arthur Tomey's ranch. There was, of course, plenty of milk and plenty of turkey, which over the summer became monotonous fare. My chores included the milking of the cows with an automatic milking machine and subsequently feeding skimmed milk to the turkeys. Whatever the virtues of the turkey as a food, it must be remembered that the turkey is a very stupid bird. Feeding the milk to the turkeys involved pouring several gallons of milk from a can into a large ceramic bowl. This was then covered with a ceramic plate and rapidly inverted and set on the

ground. Milk would then flow into the plate from which the turkeys would consume it. In those primitive times, dungarees were not equipped with zippers. Flies were closed with bone buttons and it would appear that bone buttons were an irresistible delicacy to turkeys. It would therefore transpire that while I was balancing a three-gallon pot of skimmed milk, trying to cover it with a plate and flip it over with minimal spillage, I would be surrounded by hordes of turkeys seeking to detach these bone buttons from my fly. This troublesome experience has given me a permanent distaste for the ranching life.

Before leaving the city of Boston I should like to share with my readers a few gastronomic notes. When we were broke and yet in need of a meal on the town, we would sometimes patronize a Chinese restaurant at #8 Tyler Street in Boston's Chinatown. I do not remember its Chinese name, but I do know that it was known to the Harvard undergraduates as "The Bucket of Blood." It featured all the usual Chinese dishes and, in addition, a fascinating automated violin that was played by four small rosined wheels which rubbed against the strings, and an assortment of small metallic fingers which were mechanically driven against the fingerboard. When we were very flush, however, we would sometimes visit the Locke-Ober Cafe on Winter Place. This restaurant, situated on a very narrow causeway one block long close to the Park Street subway station, was and is, in my judgment, one of the finest eating places in the United States. It was already an ancient and well-established restaurant in my time. The main room downstairs was reserved for men only, the reason being a quaint Victorian painting of a nude female known affectionately as "The Nekked Lady," who had been toasted by generations of Harvard undergraduates and their friends. One wall of this room was occupied by a very long mahogany bar that during prohibition time was used for the service of food rather than of liquor. Food was prepared with loving care and was served by thoughtful elderly waiters who had lived their lives in this same room. Featured were clear turtle soup, lobster thermidor, and wonderful fat oysters on the half shell. I last visited Locke-Ober's a few years ago in the company of my Harvard undergraduate son, and I may report that both the charm of the establishment and the quality of its food and service had not deteriorated. May it continue in its glorious tradition forever.

In June 1930 I graduated from Harvard College, B.A., magna cum laude, and was admitted to Phi Beta Kappa. The commencement ceremony then, as now,

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featured the award of honorary degrees, and I recall that one of the recipients of such a degree in 1930 was Walt Disney. It was the duty of the Harvard president to devise neat and pithy citations for this purpose. In welcoming Dr. Disney to his rank, President Lowell said, "He labored like a mountain and delivered a mouse."

Chapter IV

OF THE MOST HIGH

The College of Physicians and Surgeons of Columbia University had moved within the preceding few years to its splendid new quarters on 168th Street. All New Yorkers remembered the site as that of the New York Giants' Baseball Park, which had been preempted by a former baseball player, Billy Sunday, who had "gotten religion" and used the old stadium for his revival meetings. Jointly with the Presbyterian Hospital, Columbia University acquired title to this large tract of land between 165th and 168th Streets from Broadway to Riverside Drive. The vast grey fieldstone building was only about 2 years old when I entered as a first-year medical student in 1930.

During the previous year I had filed applications to medical schools and was pleased to receive acceptances both from Harvard and from P & S. My choice was a difficult one. My natural preference was for Harvard, which in my judgment did then, and probably still does, enjoy the highest prestige among American medical schools. The situation was complicated by the fact that my parents at that time were in the throes of a moderately bitter divorce, and my mother, under the care of an old family friend, the psychiatrist Dr. Menas Gregory, had been strongly advised to remain in New York City which was where most of our friends and family were located. Since it was my father's misdeeds which were the immediate cause of the divorce, my own sympathies were strongly with my mother, who was clearly the injured party. I therefore felt obliged if at all possible to reside in New York and regretfully wrote to the then dean of admissions at Harvard, Worth Hole, of my inability to stay in Boston. Whereas I would certainly have encountered a different series of problems and personalities had I opted for Harvard, my decision had compensations. Not the least of these was the fact that the Department of Biochemistry at P & S at that time was clearly the most productive and the most exciting in the United States, and it was with this department that I early affiliated myself. Over the portal at 630 W.168th Street is the cryptic inscription, "For of the Most High Cometh Healing." Just inside the portal was a counter leading to a cloakroom, superintended at that time by George and Charlie. These two elderly guardians had watched the doorway to P & S since long before its move

from 59th to 168th Street. In fact, they had been on duty when my father was a medical student. They promptly spotted me as my father's son and immediately regaled me with family anecdotes, including the number of overcoats that my father had owned during his medical school days. George's last name I no longer recall, but Charlie's was Costello, one of the many Irishmen with a Spanish last name derived, presumably, from the wreckage of the Spanish Armada on the Irish Coast in 1588. George and Charlie were everybody's friends and they continued for many years to serve the student body of P & S. Their names are now memorialized in a scholarship fund created at the time of their retirement. The dean at P & S at the time of my admission was William Darrach, a distinguished senior orthopedic surgeon. It was he who had interviewed me for admission. I recall that he was pleased by the fact that my chief outside interest was magic. Most of the interview was devoted to his inquiry as to how a particular trick that he had once seen was performed. He could remember neither the exact nature of the trick nor the name of the performer, and I was therefore unable to give him any useful information. Nonetheless, the interview apparently was successful.

The first year of medical education in 1930 was devoted overwhelmingly to gross anatomy. The distinguished senior faculty of the anatomy department included Phillip E. Smith, an early endocrinologist, and Samuel Detwiler, a developmental biologist. But neither of these would soil his hands with the human cadaver. The teaching of gross anatomy was delegated to an orthopedist, Dudley Joy Morton, whose reputation rested in large part upon his earthshaking volume Oh, Doctor, My Feet! Assisted by a young German surgeon named Singer and an elderly retired surgeon named Gallaudet, we the students were initiated into the charnel house. We were broken down into groups of four for this purpose, and since the listing was strictly alphabetical I was not surprised to find that I shared a dissection table with Taylor, Stevenson, and Smith. The four of us lived closely together for the next four years. Peeking into the future we see both Earl Taylor and Gordon Stevenson becoming surgeons and dying young. Gordon, the only other redhead in my class, was also the only classmate who was married during his medical school days. He became a member of a group practice in Summit, New Jersey, and by a strange coincidence was called upon to treat my niece, Wendy Weston, as a baby. Chesley Smith, when last heard from, was still engaged in the practice of internal medicine in Tarrytown, New York.

Armed with Gray's famous Anatomy and Sobotta's Anatomical Atlas, we went to work testing out our newly acquired dissecting instruments. For me it was always a rather revolting experience. In the course of the year we dissected two cadavers. The first was for the identification of the grosser elements of gross anatomy--the skeleton, the skeletal muscles, the organs and viscera, and the major vessels, while the second dissection was devoted largely to the blood supply and enervation of the several parts of the body. Dissections were very thorough and time consuming. Usually two of us would stand, scalpel in hand, while the other two would pore over the appropriate volumes, trying to read the relevant passages. The aroma of rancid fat and slightly deteriorating flesh, together with the penetrating stink of formaldehyde, contaminated the large dissection room, our books, our clothing, and our persons. It was at this time that I changed the habit of a lifetime, taking my dally shower before dinner rather than, as I had always previously done, at bedtime. Throughout the year's exposure I never came to enjoy the gross anatomy laboratory.

Each of us was supplied with a wooden box containing a disarticulated skeleton, while articulated skeletons for our study hung from hooks around the wall. Thorough familiarity with the bones, their articular facets, and the points of attachment and insertion of the several muscles was rigorously required and we were subjected to repeated tests of our knowledge. At that, the requirement was not as strict as it had been in my father's day when each student was forced to select, by touch alone, any desired bone from a collection of wrist and ankle bones. Indeed, my father reported that there was one student who could thrust a collection of these small bones into his mouth and spit out on demand whichever was called for. It is not easy to conceive of a use for this remarkable talent.

The burden imposed upon memory was very considerable, and to assist in the mastery of gross anatomy, medical students had devised a number of mnemonics. Some of these were funny, some were bawdy, and some were actually useful. When years later it occurred to me that there might be a purpose in collecting and publishing medical school mnemonics for the benefit of future generations, I felt obliged to secure clearance with my then boss, Dr. Walter Palmer, previously chairman of medicine at P & S, and at this time director of the Public Health Research Institute of the City of New York. After I had explained to him my purpose, he, a dignified and elderly gentleman, got a faraway and dreamy look in his eye and then pronounced the following sentence: "Many

Spanish ladies cannot pee, therefore they must urinate." I recall responding, "I beg your pardon, Dr. Palmer. What was that?" And he repeated the sentence, "Many Spanish ladies . . ." "What," I cried, "is that"? "That," he responded, "is the mnemonic for the names of the bones of the wrist that I learned 50 years ago." And in truth, when I finally ran down the old pre-Baseller nomenclature, the names did concur with the capital letters of Dr. Palmer's mnemonic. It is noteworthy that although he vividly recalled the mnemonic, he was totally unable to produce from his memory the names of any of the bones of the wrist.

In contrast to gross anatomy, the remaining courses offered in the first year at P & S were relatively mild and devoid of emotional impact. Histology was taught rather dryly by Phillip Smith. It consisted largely of the memorization of a collection of microscope slides so that each student could rapidly identify each organ or tissue from its histological picture. We learned, for instance, that the parotid gland looked very much like the pancreas except that the latter did contain eyelets which were of course the source of insulin. We became skilled at distinguishing between skeletal and cardiac muscle, between a Peyer's patch and an appendix. For the final examination, the faculty borrowed all of our microscopes and set them up in rows with an unlabeled microscope slide under each one. At the sound of a bell the students were required to progress every 30 seconds from one microscope to the next and write down on a strip of paper the tissue or organ in each preparation. The procedure had about the same intellectual content as the identification of postage stamps.

Neuroanatomy was rather more fun. The course was given by the entire very strong Department of Clinical Neurology and Neurosurgery with the participation of an unusual man of great wisdom, Oliver Strong, a non-physician who had an encyclopedic knowledge of neuroanatomy. He was a dour, elderly man with grey hair, steel-rimmed spectacles, and a surprising enthusiasm for the early sex goddess of the movies, Clara Bow. We learned of the tracts in the spinal cord, of the nuclei of the brain stem, and the gross structure of the brain itself. One reason for the great interest of the students was that in this course and in this course alone were we exposed to an occasional patient. I well remember the first patient whom I ever saw. It is worth noting that upon inquiry of many other physicians, I have found that almost all doctors remember throughout their lifetimes their first clinical exposure. In my own case it was a patient presented by the neurosurgeon, Byron Stookey. The patient exhibited a total loss of all pain- and temperature-sense below the level of the lumbar spine.

Otherwise he appeared to be neurologically entirely normal. The problem presented to the students was to localize the lesion which might produce these signs. Clearly, no one lesion could do this, and I guessed that this patient had two separate and discrete lesions, each one involving the spinothalamic tract, left and right. This, in fact, is what the patient turned out to have, but what we were belatedly told was that the lesion had been surgically induced by Dr. Stookey who had cleverly inserted his scalpel into the spinal cord on both sides so as to divide this pathway. The purpose of the procedure was, of course, to control otherwise uncontrollable pain in the pelvis and lower extremities. I shall not forget the patient, nor yet my satisfaction at correctly guessing the location of his abnormality. Particularly I shall always remember Dr. Stookey's obvious pride in the skill with which his procedure had been completed. There was no evidence whatsoever that he had nicked a single fiber of the adjacent pyramidal tracts.

For me, obviously the most satisfying course in the first year was biochemistry. This department was headed by Hans Thatcher Clarke, whom I have mentioned in an earlier chapter. He was a very benign gentleman, a humanist and a musician, whose training had been in organic chemistry. He had studied in London and in Berlin, where he worked in the laboratory of the great Emil Fischer. As a graduate student in Fischer's laboratory, he had actually prepared the first sample of mustard gas and had discovered some of its unpleasant properties by accidentally spilling some over his skin. He had returned to the United States during or shortly after World War I to assume direction of the Eastman Kodak project to develop a substantial catalog of organic chemical substances for the marketplace. Prior to that time, most organic substances that might be required in American laboratories were imported from Germany. It now became essential for the United States to achieve an independent source of these materials. The Eastman Kodak Company, in Rochester, New York, undertook this job and, under Clarke's direction, produced for the market a long list of organic chemicals. It was from this position that Clarke had been brought a few years earlier to head the Department of Biochemistry at P & S. The emphasis that he brought to biochemistry was clearly that of the synthetic organic chemist. His knowledge of biology and physiology was very limited and he shunned the more biological aspects of the field. His judgment on matters of organic synthesis and on the criteria of purity of organic substances was superb, and as mentioned earlier, he had an uncanny ability to identify compounds by their odor. His behavior was

always calm and unruffled as was his personal life. He and Mrs. Clarke, a daughter of the great Max Planck, lived with their four children in a large home in Riverdale in the Bronx, a community that was popular with the P & S faculty. The subject matter of biochemistry in 1930 dealt largely with the chemical composition of the tissues and fluids of the body and with the essential and nonessential ingredients of the diet. Nutrition was in its heyday. Studies conducted particularly at Yale University and at the University of Michigan were completing the list of essential amino acids. The structures of the B vitamins were even then being unraveled and the roles of these interesting substances were still unknown. I can vividly recall several years later reading the important paper of Lohmann and Schuster, which enunciated for the first time the principle that the B vitamins served as parts of co-factors for important enzymes. The Department of Biochemistry at P & S, although quite advanced in some areas, was slow to catch on to the developing field of enzymology, which was being created in Europe by Meyerhof, Embden, von Euler, and Warburg. Doubtless because of Clarke's interests there was more stress on the structural aspects of biochemistry, which at that time included classical studies of the structure of porphyrins, sterols, bile acids, and the simpler hormones thyroxine and epinephrine. The course for medical students, which was in fact the only course that the department sponsored, was a combination of lectures and laboratory exercises. Much of the latter was devoted to the properties, color tests, and analytical methods for the many constituents of the tissues and body fluids. We learned to distinguish sugars one from another and were given "unknown" sugars to identify. I recall that each student was supplied with a quantity of wool, from the acid hydrolysate of which he was required to prepare and recrystallize samples of the amino acids cystine and tyrosine. While the skills thus learned proved to be of some use to me in my own career, I am certain that they were of no value whatsoever to the vast majority of my clinically oriented classmates.

The remaining course in the first year of studies was human physiology. Of the chairman of the department, Dr. Williams, I have only scanty recollections. He was an early student of the electrocardiograph, having worked in Holland in the laboratory of Einthoven. He had set up at P & S what purported to be the first American electrocardiograph, which involved a very massive Einthoven quartz fiber galvanometer, backed up by a roomful of controls and accessories. With this machine he was able to produce electrocardiographic

tracings, then a remarkable novelty. Another member of the physiology faculty was Professor Scott who, it was rumored, had isolated samples of insulin prior to the 1921 isolation which won the Nobel Prize for the Canadian team that included Banting and Best. Scott, however, failed adequately to publicize his discovery and as a result was one of the "forgotten men" in the history of diabetes. My friend Charlie Best, in historical lectures delivered in his latter years, reviewed this extraordinary piece of history from which it appeared that insulin was discovered and rediscovered a number of times before the truth of the discovery finally burst upon the scientific world. The junior member of the department I remember very well--K. C. Cole, universally known as Casey. He was an early electro-neurophysiologist and the inventor of the "voltage clamp," a research device of great importance in his field. I recall that his lectures were essentially totally incomprehensible to the student body, since they seemed to involve a 3-dimensional representation of the electrical phenomena which occurred during and after an action potential but always presented in a series of 2-dimensional projections from which the student was required to reconstruct the 3-dimensional image. This is a formidable task if one thoroughly understands what one is trying to do, and an impossible task in all other circumstances. Nonetheless, Casey was a man of great good cheer, a gifted physiologist, and a good teacher in the one-on-one situation. I was pleased to re-encounter Casey when I came to the National Institutes of Health, where he had established himself as one of the principal investigators in the Neurology Institute. We still continue to see him during our summers at Woods Hole, where he is a senior scientist and has laboratory space in that corridor devoted to the study of the giant axon of the squid known as Squid Row.

The laboratory exercises in physiology in that era still depended heavily upon the kymograph, a recording device based upon the use of a strip of white paper carefully coated with lamp black. A variety of delicate pens actuated by various mechanical devices left tracings on this strip of paper as it slowly moved, driven by a clockwork motor. The machinery was, by today's standards, unbelievably primitive and remarkably unreliable. I recall that the respirators, which were the basis of the anesthesia equipment, were manufactured from the motors of auto windshield wipers. Cats in considerable number were sacrificed to the teaching of physiology. We were required to perform elaborate plumbing operations involving cannulae in the carotid arteries, the tracheas,

and other viscera. The course served, among other things, as an introduction to animal surgery.

Looked upon in retrospect, medical education in 1930 was still in the encyclopedic phase. The student was expected to amass a substantial fraction of all available medical knowledge, and this was still possible because the available knowledge was, by today's standard, quite limited. Nonetheless, it was a formidable undertaking and consumed all of my days and most of my nights.

The summer of my first year in medical school I spent as a guest worker in the Department of Biochemistry. Here I was given bench space in the large laboratory that housed all the graduate students, of which there were approximately one dozen. These became my close friends and associates during my stay at P & S. I was particularly attracted to Sam Gurin, who at that time was earning his way through graduate school by serving as a technician to Williams and Waterman, the co-discoverers of thiamine or vitamin B₁. Since it was known that thiamine deficiency, or beriberi, developed when humans or chickens were fed polished rice, and that the disease could be corrected by feeding whole rice kernels, the rice polishings were regarded as a likely source of the vitamin. It was Sam's job to shovel literally tons of rice polishings into large extraction equipment which R. R. Williams had designed for the purpose, and from these extracts was derived a crystalline product, thiamine hydrochloride. Its structure proved difficult to elucidate until Hans Clarke, chairman of the Department of Biochemistry, identified the thiazole ring from the odor of one of the derivatives. The firm of Merck was licensed to develop the thiamine extraction process for large-scale production, but this proved troublesome. As a result, much time and money were wasted in preparing the first batch of thiamine suitable for clinical testing. By that time I had matured to the level of medical intern at Bellevue Hospital and was pleased to serve for one month as the medical intern to the Alcohol Service of the Bellevue Psychiatric Hospital. The director of that service, Dr. Norman Joliffe, presented to me one day an ampule of crystals which Merck had sent to him for testing and which was said to be the first batch of crystalline product that Merck had secured. It fell to me to inject this material intravenously into an old chronic alcoholic patient who had severe peripheral polyneuritis. This patient had been repeatedly examined by members of the staff and no one had, in the past several admissions, been able to elicit a knee jerk or any other deep reflex. With trembling hands I cracked open the ampule, dissolved its contents in distilled water, and injected the

solution intravenously. To our deep gratification, on the next day the patient was found to have active knee jerks and ankle jerks. Norman Joliffe was bubbling with enthusiasm and suggested that we at once write a brief clinical report. Fortunately we did not do so since, on many subsequent trials of thiamine in this situation, we were totally unable to repeat this dramatic result.

Sam Gurin was far more than a shoveler of rice polishings. He was also a gifted musician who played the piano--both classical and jazz--with remarkable ease, and he was therefore in high demand at social gatherings. He was the sheet anchor of our own local quartet which included Joe Victor, G. L. Foster, Oskar Wintersteiner, and possibly others. On these occasions Sam would play the piano or the cello interchangeably. In later years, Sam added musical composition to his many accomplishments. Sam's subsequent career took him to the University of Illinois for a while, and then to the University of Pennsylvania where he served both as Chairman of the Department of Biochemistry and as Dean of the Medical School. Finally, he moved to Florida where he established a marine biological research center for the University of Florida in the town of St. Augustine. His most recent studies have had to do with the chemotaxis of mollusks. When I first knew Sam he had two problems. One was the fact that he was working for a Ph.D. degree with Hans Clarke on a tedious problem that had to do with the identification of the basic amino acids in protein hydrolysates. This he accomplished by the then novel method of toluenesulfonation. Sam's other problem was that he had married a beautiful young woman named Celia, but had not had the time or funds to take her on an adequate honeymoon. It was my good fortune at that time to be the proud owner of a small Ford Model A coupe, and it was decided that I should take the Gurins on a honeymoon tour of the Gaspe Peninsula, the southern lip of the mouth of the St. Lawrence River, then a relatively primitive and inaccessible section of Canada. Lewis Engel, also a graduate student in the department, was going to be on the Gaspe Peninsula with his family at one of the elegant resort hotels. We therefore packed into my car and had a hilarious adventure together. The language spoken on the Gaspe Peninsula was Canuck, a strange and degenerate version of French which possibly traced its origins to the 17th and 18th centuries. We stopped at odd inns and farmhouses, went fishing with the natives, saw some remarkable scenery, and traveled over some terrifying cliff-hanger and unsurfaced roads. We did, however, complete the trip successfully and have been firm friends ever since.

My project during that summer was, in retrospect, very naive. I had found some references in the literature which indicated that the phenomenon of fibrinogen conversion to fibrin might require the participation of gaseous oxygen, and I therefore undertook to study this reaction in the anaerobic state. I was unable to adduce any useful data from the crude experiments that I designed. It was, however, my introduction to a sophisticated biochemistry laboratory environment and I found that I liked it very well. Particularly was I fond of the kinesthetics of the laboratory--the manipulations, the setting up and knocking down of complicated equipment, the glassblowing, the wiring, the plumbing, and all the other things that go into experimental science.

The second year at P & S was devoted chiefly to pathology, pharmacology, microbiology, and physical diagnosis. Of these, pathology was clearly the main topic, and once again we were given a large box of slides--in fact, several boxes--with the assignment of committing them to memory. Pathologic processes were briefly described but the main point of the game was the recognition of the end state. Pharmacology was rather more fun, partly because the chairman of the department, Dr. C. C. Lieb, had personally invested substantial amounts of money in elegant equipment. Each group of four students was supplied with the most modern and complex motor-driven kymograph, and large numbers of dogs, cats, and turtles were sacrificed on the altar of education. Once again our team was composed of Taylor, Stevenson, Smith, and myself, and we found that we worked together very easily. For each of a large number of drugs we had to learn the essentials of action, the dosage, and the modes of administration. We even received a course in prescription writing, which proved to be the only useful application of the many years I had earlier invested in studying the Latin language. Microbiology was taught by Professor Gay and his staff. It dealt almost entirely with the descriptions of the pathogenic bacteria, their separation and identification, which was based chiefly upon the sugars that each bacterium did or did not ferment. Viruses were touched upon lightly and the bacteriophage phenomenon was briefly introduced. Immunology at that time was a very primitive and elementary subject and was taught chiefly at the applied level. After we had learned the relatively simple maneuvers of flaming a platinum wire loop, unstoppering a sterile culture flask, and streaking an agar plate, we were entrusted with a variety of pathogenic microorganisms in various teaching exercises. The text of the subject by Topley and Wilson was in two volumes bound in bright blue cloth, and I spent many hours assimilating its

contents. We all learned and then promptly forgot the life cycles of the several protozoan parasites of medical importance, and for the most part none of us ever saw these organisms again.

Finally, in the second year we were introduced to the problems of patient contact. We were taught history taking by Dana Atchley and physical examination of the patient by Robert Loeb. The latter instruction started by pairing off of students and percussing each other's chests, auscultating each other's hearts and lungs, and palpating each other's abdomens. Armed with our brand new stethoscopes, ophthalmoscopes, percussion hammers, a safety pin, and a tongue depressor, we now began to feel ourselves to be real physicians. We carried our diagnostic instruments with pride. I recall that the entire class was taken by bus on a number of occasions to a large hospital on Staten Island where there were many patients suffering from chronic pulmonary tuberculosis, a truly dread disease in those days. It was a useful disease for the purpose because it produced extraordinary physical signs which could be heard and seen by the veriest dodo. We soon learned to distinguish between the various kinds of rales and to recognize resonance, dullness, and tympany. The several cardiac rhythms and murmurs proved to be somewhat more elusive, but the caustic tongue of Dr. Loeb provoked us to listen more acutely to the strange noises that were coming up the tubes of our stethoscopes. He was a demanding taskmaster and a superb teacher. During the summer after my second year of medical school, I went to Germany to work in the Pathological Institute at the University of Freiburg. This experience was described in Chapter 1. While in Freiburg I attended the magnificent lectures of its reigning guru, Geheimrat Ludwig Aschoff. He was, bar none, the finest lecturer I have ever heard. This was in part due to his unusual wisdom and his great literacy. It may also have been in part due to the curious German system which made his earned income contingent upon the number of students whom he attracted to his lectures. The fact that German medical students were free to drift from one campus to another, combined with the curious capitation system for reimbursement of the faculty, tended to place a stress on teaching skill for which there is no counterpart in American medical schools. He regarded the process of disease as a struggle. The microscope slide usually represented the end stage of the struggle, but what was really interesting was the process. Tuberculosis to Aschoff was not merely a histological picture, although this of course was important. To him it was an ongoing fight between the tubercle bacillus on the one hand and the host human

on the other. This he described with all the eloquence of America's then great sports radio commentator, Graham McNamee. He kept the students on the edges of their seats in the excitement of the conflict. Aachoff was not a man who spared himself. Though small of stature and slightly asthmatic, he would pick up enormous museum jars in which pathological specimens were exhibited, carrying these rapidly from one end of the podium to the other so that every student would have an opportunity to inspect the contents. I recall his pointing to such a jar and shouting out so that everyone would hear: "Carcinoma der Leber, Carcinoma der Leber, Carcinoma der Leber" (cancer of the liver). For the first time I appreciated the excitement of pathology. This, which had been a rather dull course at P & S, was very dramatically presented at Freiburg.

On my return home I entered the third year at P & S. From here on the curriculum was entirely clinical. It was so arranged that the bulk of the third year was spent as a clinical clerk on each of several ward services at Presbyterian and other affiliated hospitals in New York City, while the fourth year was spent in the outpatient departments of Vanderbilt Clinic. The outpatient experiences, though permitting diverse exposures in the medical and surgical specialties, I found rather unsatisfactory. Far more interesting to me were the clinical clerkships, particularly that on medicine with Dr. Dickinson Richards. Every morning we made rounds together, each student presenting to Dr. Richards his new patients and new findings on his older patients. These would be discussed in detail by the instructor, the intern or resident, and the group of medical students. We came to know our patients very well and we learned necessarily the format for the presentation of the clinical problem. We were under continuous scrutiny by the faculty of medicine and we tagged along on grand rounds when the chairman of medicine, in those days Dr. Walter Palmer, made his weekly inspection of the entire medical service. Grand rounds were an awesome experience involving participation of the entire Department of Medicine with the clinical clerks following along behind. Incidentally, in those days we actually marched physically from bed to bed, the wards of Presbyterian Hospital having about eight beds in a typical room. Walter Palmer, whom I came to respect and know far better much later in my career, was not an exhilarating rounding physician. In fact, grand rounds, except for occasional flashes of brilliance from Drs. Loeb and Atchley, were fairly tiresome. Dr. Palmer had earned for himself the name of "shifting dullness," a physical sign which is elicited when there is fluid in the peritoneal cavity.

Although I never had much difficulty in securing good grades during my academic training, I never felt truly at home in the one-on-one experience of clinical practice. I knew right from the start that I felt more at ease in the laboratory than at the bedside, and specifically that I had no interest in a career in the cutting arts--surgery, gynecology, and obstetrics. True, as a medical student I delivered my eight babies, as was set forth in the regulations. This was done mostly at the Morrisania Hospital in the Bronx where, again together with my three alphabetized classmates, we covered the obstetrical service nights until we had completed our required experience. I approached the whole business with considerable anxiety and failed to derive the deep satisfaction which some of my classmates appeared to secure from the experience.

During the last year of medical schooling, everyone was deeply concerned about internship and residency training. Advised by my old Boston sponsor, Frank Fremont-Smith, I applied at the several major Boston hospitals--the Massachusetts General, the Peter Bent Brigham, and Boston Beth Israel. However, graduates of P & S had not had much success in gaining admission to these three hospitals, nor did I. Having failed to secure a Boston internship, I was happy to accept an appointment on the Third Medical Division of Bellevue Hospital. This was the division closely affiliated with New York University School of Medicine, which was located directly across First Avenue from Bellevue Hospital. We all felt that it was the most carefully attended and the best of the four divisions of which Bellevue Hospital was composed at that time. The First Division was Columbia, the Second Division was Cornell, and the Third Division was New York University. The Fourth Division was considered an open division and had no close affiliation with any medical school, and there was some friendly rivalry among the interns and residents assigned to each of these divisions. My internship started on July 1, 1934, and my first night on service was July 4. It was on that evening that I acquired my deep and lasting respect for firecrackers and for the damage which they can do. But more of this in the next chapter.

Chapter V

BELLEVUE HOSPITAL

On the east side of First Avenue, between 26th and 31st Streets in Manhattan, stood the ancient brick pile that was Bellevue Hospital. It was surrounded by a tall iron fence and fronted directly on the East River, which is Manhattan's most interesting river frontage. The large boat wharf of the New York Yacht Club was at the foot of 26th Street, whereas a few blocks away on another wharf stood the Municipal Lodging House, an overnight accommodation for the abundant destitute of New York City and a source of many of our patients. Bellevue was the largest and most distinguished of the hospitals of the City of New York. It had 2,400 beds, a vast outpatient department, a relatively new and handsome psychiatric pavilion which had been constructed by our old family friend, Dr. Menas Gregory, with the support of his sponsor, Mayor Jimmy Walker, New York's famous playboy mayor. It also housed the city morgue and the office of the medical examiner, which was responsible for autopsies on all persons who died under auspicious circumstances in the city. It had a most active emergency room which was fed by a busy ambulance service covering a band across Manhattan between 42nd and Houston Streets, river to river. In addition to the usual services of medicine, surgery, pediatrics, obstetrics and gynecology, it housed an active alcoholic pavilion, a fascinating prison ward, and a gloomy erysipelas ward. It was, in a sense, a hospital of last resort. Other hospitals in the city had the privilege of rejecting new admissions when all of their beds were filled. Bellevue did not have this privilege. No one could be denied admission, and consequently there were often rows of cots set up between the rows of beds on its wards. It was, in the opinion of its interns and residents, the most exciting hospital in the world.

Because of ancient historic ties (the origins of New York University's School of Medicine were, in fact, rooted in Bellevue Medical School), and because NYU Medical School actually sat across the street from Bellevue Hospital, the Third, or NYU, Division was the most active teaching service. It was therefore deemed to be the preferred service for internship. On July 1, 1934, I appeared at Bellevue Hospital for my initiation. We were greeted by the Dean and Chairman of Medicine, Dr. John Wyckoff, who turned us over to his

chief medical resident, Dr. Joseph Bunim. Joe instructed us briefly in our duties, and then referred us to the laundry room where we were issued an array of short white coats, white shirts with Russian-style collars, and white trousers. The white socks and shoes, which completed my uniform for the next 2 1/2 years, we were supposed to supply ourselves. We were each assigned a very small private bedroom, were introduced to the large dining hall, and were told that our stipend from that time forward would be \$7.50 each month. As interns, we were on duty every day and every other night with the exception of alternate weekends. The internship lasted one year and was evenly split between service on the medical wards and service on the surgical wards. My time was mostly spent in the A and B building which fronted on the East River. The fifth and sixth floors of this building were devoted to the Third Medical Division. My medical ward, as I recall it, was 5A. This and every other ward in the building had 26 iron beds, 13 on each side of the long room. There was no other furniture in the room except for the nurse's desk, an enameled iron affair lighted by a desk lamp with a green glass shade. Here sat a nurse all day and all night, updating the charts of the several patients, preparing medications for distribution, greeting the new admissions, assisting patients at discharge, and responding to calls from patients in bed. Normally the charge nurse would be supported by another nurse, one or two student nurses, and an orderly whose major task was to pass out and collect bedpans. Movable screens were available to secure a minimum of privacy for each patient, but these were often not used. The wards were light and airy, were equipped with porches that could be used by the patients in the summertime, and harbored the largest cockroaches I have ever seen. We were early instructed not to step on the cockroaches because it was their duty to reduce the population of bedbugs, a far more troublesome pest. Despite all these handicaps, it is my recollection that the nursing services were superior and the medical skills were actually the best available. It was chiefly the comforts of life that were lacking, and of these the most striking deficiency was privacy. Virtually everything was done in public and every patient on the ward knew precisely what was happening to every other patient. Whereas the normal patient load was about 26 patients, during influenza years in the wintertime one or two rows of cots running the entire length of the ward would sometimes double this population. The corridor which separated the A and B wards had a number of small rooms, including a minuscule clinical pathology laboratory, a small leaky X-ray machine and adjacent

darkroom, and one semi-private room for the occasional VIP or a moribund patient who was best separated from the general commotion.

Each medical ward had an assigned faculty member in general charge. There was, in addition, an intern assigned to each ward, while each pair of wards had a junior and a senior house officer. These latter were, respectively, in the second and third years of their residency, and whereas they shared our food and housing and enjoyed the same stipend as did the interns, they did have one important perquisite: they were on call only one night out of four instead of one night out of two. All interns aspired to these lofty positions. Every morning the intern and his attending physician would make rounds, inspecting every bed on the ward. There was a host of medical specialties, each one served by its visiting physician. Thus we had a cardiac service, a renal service, a diabetes service, an endocrinology service, etc., and representatives of these services would drop in during the morning to see the patients in their particular provinces. It was the duty of the intern to be thoroughly familiar with every patient on his ward and to make sure that the diagnostic workup and the course of therapy prescribed were being carried out. Rounds in those days were a pedestrian occupation for the staff. We walked from bed to bed, and to facilitate this process everything that related to a particular patient was at his bedside. His chart was clipped to the foot of his bed. All of his X-rays would hang in a large manila paper envelope fastened to the foot of his bed by bandage ties. His electrocardiographic tracings (in those days we only took three leads) were actually incorporated into his chart. The front page of his chart was a graph with two lines, one in red ink, the other in blue, one revealing his temperature, the other his pulse rate. Beneath this graph there was space for urine and blood analytical data. The nurse had the responsibility of plotting the temperature and pulse curves, while the intern had the responsibility of filling in the appropriate analytical information, and woe betide the intern who was negligent in this duty. Each newly admitted patient received a complete workup, including a complete history and physical examination, as soon as he got to his ward bed. This function was actually carried out in duplicate by a clinical clerk from NYU and by the intern. One of the pleasures of the intern's life was to share his vast medical knowledge with the naive third or fourth year medical student. Then the next morning on rounds, either the medical student or the intern would present the case verbally to the visiting physician. The patient, where indicated, would then

be referred to one of the specialty services for consultation. The assembling in one place of the patient, his chart, his EKG tracings, and his X-rays made for coherent teaching and prompt evaluation, which is, in my opinion, not matched by present hospital practice that places the patient in his bed, the chart in the nurses' station, the X-rays in the Department of Radiology, and the EKG frequently lost in transit.

Most of the patients in this vast city hospital in 1934, at the height of the great depression, were destitute. Frequently the only home address they could give was the Municipal Lodging House. Many were malnourished, many were alcoholic, and not a few were addicted to heroin which was the only street drug of that era. As mentioned earlier, whereas other hospitals might deny admission to these sometimes troublesome patients, Bellevue Hospital was required by law to provide services to them.

Here it was that I came to work in July of 1934. I suppose that I was on call for the night of July 2, but I have no memory of what may have happened. On the other hand, I do recall with considerable anguish the night of July 4, for it appeared that on that night every child living in the Bellevue Hospital ambulance district managed to burn his fingers or body on a firecracker. Because such burns were a notorious source of tetanus infection, every such victim brought into the hospital had to be given a shot of tetanus toxoid. Most of the patients were given their shots and then, after their wounds had been cleaned and dressed, were discharged. The numbers of patients seen in the emergency room that night must have run into the hundreds. The pharmacy depleted its supply of tetanus toxoid and we were forced to send a motorcycle policeman to other city hospitals to scavenge this precious material. That night I never got out of my uniform, and by the next morning I was well conditioned to the life of a Bellevue intern. I never really recovered from this initial fatigue for the next 2 1/2 years.

A man of key importance in the operation of a large city hospital is the admitting physician. Whereas there must have been several persons sitting in this office during my term at Bellevue, I only remember one and his name was Dr. Cutolo. Because of the nature of his job, he had developed an extraordinary facility for rapid evaluation of incoming patients and instantaneous diagnoses, sometimes right, sometimes wrong. It was of more than passing interest to me to observe how a diagnosis, once attached to a patient, could be detached only with the greatest difficulty. Thus, one day Dr. Cutolo was confronted

with a middle-aged male patient, obviously acutely ill, suffering from severe headache, moderate fever, and a generalized body rash. The man gave a history of having resided in a house infested with rats, and based upon that single statement Dr. Cutolo made the unlikely diagnosis of possible typhus. The patient was sent up to our ward, and in pursuit of diagnosis a variety of tests were performed-- among these the Weil-Felix reaction. This was a test for infection by the Rickettsia of typhus and other related organisms. It was part of the routine workup for patients who had fevers of unknown origin, and in my experience the results had always been negative. On this particularly patient, however, the result came back positive, thus fixing in all our minds the diagnosis that Dr. Cutolo had ventured. However, the course was uncharacteristic. The fever subsided, the headache subsided, but the rash persisted. Finally we called for a consultation with our senior dermatologist, an elderly Armenian physician, Dr. Parsegian, and he noted something which had escaped the attention of all of the other observers--namely, that clearly inscribed on the front page of the chart was the result of the patient's Wasserman test, 4+. Dr. Parsegian then pointed out that the rash extended over the palms of the hands and the soles of the feet, which is a characteristic almost peculiar to secondary syphilis. A hurried consultation with the textbooks revealed that secondary syphilis is one of the relatively few conditions which may give a false-positive Weil-Felix reaction.

Much of the drama at Bellevue Hospital started in the emergency room, a relatively well-appointed ward adjacent to the admitting office. Here were brought most of the patients from the ambulance service, which included all of the usual medical and surgical emergencies: diabetics in coma, myocardial infarctions, street accidents often with fractures, acute surgical conditions of the abdomen or thorax, victims of knifings and gunshot wounds, and patients in coma for various reasons. The ward, as I vividly recall, was dominated by a superb nursing staff led by three sisters who had somehow captured this most glamorous of nursing positions. Here one often met the persons who would be featured in tomorrow's headlines. It was the natural spot to which interns with nothing else to do would gravitate. Also, the press usually sent a representative to this room every evening to find out what was happening. Whereas in Bellevue, as in many other institutions run by the City of New York, there were many examples of incompetence and corruption, in the

emergency room everything usually worked very well. It was a room of crises and I should like to recount two experiences which occurred during my stay.

The Church of St. Mark's in the Bowery is one of New York's oldest. It was here one evening during a wedding ceremony that a disastrous flash fire occurred. The hall had been hung with highly combustible paper decorations which somehow were ignited, and within a matter of seconds the entire company was scorched. The damage was particularly severe to the women in the audience, since they were in décolletage and unprotected. All of the burn victims, including the bride and groom, were brought into the emergency room of Bellevue Hospital. Within a period of 10 or 20 minutes the entire staff was mobilized and everyone promptly went to work. Gone were the arguments between interns and nurses, gone were the jealousies and rivalries between the several medical and surgical divisions. A job had to be done, it had to be done quickly, and one sensed that there was an awakening of the soul of Bellevue. It was an exciting and inspiring evening. Wounds were dressed, infusions were started, analgesics were administered, and by early morning the emergency room, though still very full, was again quiet.

Another occasion that I shall never forget was the burning of the Caribbean cruise ship Morro Castle. Heavily laden with a vacation crowd, this ship was headed for the Caribbean out of New York when it caught fire. When all attempts to put out the fire failed, the captain decided to drive the vessel up on the beach at Atlantic City, and this maneuver was successfully completed. Passengers and crew were assisted from the ship, but many of them jumped overboard to be picked up by rescue vessels. The Coast Guard was mobilized, and since the local hospitals were of limited capacity it was determined to transport most of the victims by boat to the city piers at Battery Park at the foot of Manhattan. Here the boats were met by all available ambulances in the city of New York, and the patients were then taken to the various hospitals. I believe some 80 patients were admitted to Bellevue Hospital within an hour, and this imposed an enormous load. The victims were in some instances burned and in others were suffering from exposure and immersion in the ocean. Some of these were seriously ill, and I recall that one victim, the ship's radio operator, was specifically assigned to the Third Medical Division and to my ward. I came to know this man very well. As a result of having imbibed large amounts of sea water, he arrived in a very edematous condition. Finally, his edema was resolved in a flood diuresis and

he was restored to good health. Some years after his discharge we were interested to learn that the cause of the fire on the Morro Castle was finally clarified. The fire was the result of arson committed by an aggrieved member of the crew, and the arsonist was said to have been the ship's radio operator. I have no way of knowing at this time whether this was actually our patient but it may well have been.

The medical service at Bellevue Hospital was devoted chiefly to acute problems. Every attempt was made to move chronically ill patients into other institutions, leaving to us the acute and often dramatic problems. We saw large numbers of diabetic patients in ketoacidosis who needed continuous attention, often for many hours, before they could be pronounced out of danger. One of the dangers in this situation was the forceful and dynamic character of Dr. Elaine Ralli, who was in charge of the diabetes service and who could verbally cut to pieces any intern whose clinical judgment deviated from hers. Fortunately I had no problems with Dr. Ralli, who was aware of the fact that I had a greater familiarity with biochemistry than she did. My relations with others of the visiting staff were not always so easy. I recall the readmission of a young Jewish male hemophiliac whom I had seen on previous occasions. At this time he was in the hospital because of some dental surgery, but he confided in me that he was intending to wed and wanted personal advice. He operated a newsstand and was more literate than most of our patient population. He had consulted books in the public library about his disease and was fully familiar with its genetics. How should he approach his marriage and what should he do about possible children? It was clear that none of his children would exhibit his disease. His sons would be free and clear, but his daughters would have a 50 percent chance of carrying the disease and of transmitting it, in turn, to their male offspring. After prolonged discussion, we more or less agreed that a reasonable course for him and his bride would be to practice contraception and to adopt children as they saw fit. Please recall that at this time amniocentesis and prenatal determination of sex were still in the remote future. The next morning our senior hematologist, Dr. Joseph Connery, a devout Catholic, visited with his old friend, the recently readmitted hemophiliac, who at once recounted our evening's conversation. Dr. Connery was furious. He first threatened to have me fired and then told me that he would bring charges against me for meddling in something that was none of my business. I recall taking strong exception to his attitude but

could think of no clever answers. At all odds, his temper, which was quick to flare up, was also quick to die down, and over the ensuing years Joe Connery and I had no further problems. Needless to say, no dramatic actions were taken.

Curiously, although most of our patients were virtually destitute, we detected no spark of revolution among them. On the contrary, they seemed to enjoy the notion that there was great wealth available in the neighborhood, and this was continuously brought to their attention by the display of enormous ocean-going yachts of the New York Yacht Club's ocean squadron which lay moored at the foot of 26th Street. Our patients came to know the names of the owners of these boats, their coats, and even their solid gold fittings. These they described to each other but we never detected a note of hostility. Perhaps the depression had beaten all fight out of New York City's poor.

Very occasionally we encountered patients of another kind. Thus, one New Year's Eve the ambulance brought to Bellevue Hospital a man with a badly comminuted compound fracture of the leg, the result of an encounter with a Fifth Avenue bus. The victim was wildly inebriated so we packed him in sandbags, gave him the paraldehyde which was then the standard medication for intoxication, and notified our consultant orthopedic surgeon. When he arrived the next morning it was clear that we had by chance caught a most unusual fish. The patient turned out to be a high executive of a tobacco company based in Raleigh, North Carolina. He had come to New York to indulge in New Year's Eve conviviality when he met his unfortunate accident. Now, having sobered up, he was able to give consideration to his future course. He inquired as to the likely length of his hospitalization and was assured that it would be prolonged. The orthopedist suggested his transfer to a private hospital--the French Hospital with which he, himself, was connected--pointing out that there he could be placed in a comfortable private room, whereas at Bellevue he would have to take his place in a large ward. The patient wisely pointed out that weeks or months in a private room would probably drive him crazy, whereas it might be rather interesting to study the workings of a ward in a large city hospital. He therefore elected to remain in Bellevue provided he could be given a corner bed and could, from time to time, order decent meals from the Hotel Vanderbilt which was not far away. These conditions were met, and as a result the patient spent many weeks on my ward. He made a relatively smooth

recovery and after a while could be entrusted to a wheelchair, a vehicle which he mastered with great skill. He came to know the occupants of every bed on the service, and whenever a new patient was being admitted, whether by day or by night, he was always right there listening in on the history and watching the initial physical examination. He kept daily notes on all activities and indicated that it was his intention to write a book on his experience. As far as I know, the book was never published. However, when he finally was ready for discharge, he invited all of the staff to a splendid party in a New York City hotel and distributed silver cigarette lighters to each of us as mementos of his stay at Bellevue Hospital.

In those days before the introduction of antibiotics, acute infectious diseases posed special problems, and one of the most dread of these was meningococcus meningitis. I vividly recall a young Scandinavian male who came to the hospital with this disease and was treated, as was then the fashion, with large doses of meningococcus antiserum administered intrathecally. We were soon relieved to find the disappearance of white cells and the reappearance of glucose in his cerebrospinal fluid but he continued to be ill. He ran a high fever and exhibited showers of petechiae, minute hemorrhages under the skin. Repeated blood cultures finally revealed that whereas his meningitis had been corrected, he had a persistent meningococcemia. The microorganisms could be grown out of his blood. Today such a situation would not present a terribly serious problem. We have a variety of antibiotics which are very effective against the meningococcus, but in 1934 or 1935 this was not the case. Our specialist in infectious diseases was Dr. Milton Rosenblueth, and he pointed to a few citations in the literature which described the successful treatment of gonococcemia by the administration of fever. The gonococcus and the meningococcus are quite similar microorganisms, and from their cultural characteristics it could be inferred that temperatures significantly above normal body temperatures would be deleterious to their growth. Since it had worked in the case of gonococcal infection, should it not be tried in the case of meningococcal infection? At all odds, we had very little choice. Our patient, having received large amounts of horse antimeningococcus serum, was now thoroughly sensitized to horse serum proteins and would tolerate no further injections.

The procedure selected was attributable to the creative electrical engineer of the General Motors Company, Charles Kettering, who had devised a machine

known as the Kettering hypertherm. This was a tentlike structure which could be placed over the patient's bed. Inside were a number of carbon filament electric light bulbs which gave off a great deal of heat. This structure could be placed over the patient, covered with blankets, and then turned on. With a thermometer in the patient's mouth, we could observe the rise in his body temperature that soon occurred. Both the intensity and the duration of each treatment were carefully controlled. After about five such treatments, we were delighted to find that the recurrent fever had now disappeared and the blood cultures had become entirely negative. We discharged our patient as cured and promptly set about to write our case report. The report was eventually published, but unfortunately for us, in the intervening period of time the sulfonamide drugs were introduced and were found to be peculiarly effective in the treatment of meningococcus infection. So far as I am aware, no one paid the slightest bit of attention to this report, my second publication.

The life's blood of Bellevue Hospital was its ambulance service. In my time there was a statutory requirement that there be a physician on every ambulance, and it therefore happened that for one month out of the surgical portion of the internship each intern served as ambulance surgeon. My month was January 1935, and during this entire month the streets of New York were covered with snow. The ambulances of that era were wide open in back and desperately cold. Bellevue ran four ambulances at a time, one assigned to each of the four surgical divisions. The drivers were very skillful and knowledgeable in the details of geography of the city. The equipment was minimal. Each ambulance had a bench along each side. On one of these the physician might sit, on the other a stretcher could be placed. We were each provided with a very heavy black leather bag containing all sorts of equipment, some of which was totally useless. We carried arm and leg splints, a substantial variety of medications, and the usual diagnostic instruments, but we had no radio contact with home base. The hospital provided us with heavy dark blue overcoats, which were presumed to keep us warm, and with a minimum of instructions as to precisely what our duties were. Anyone in New York could at that time pick up the telephone and call for an ambulance. It was generally believed that on such a call you got your nickel back from the telephone company. The call was simultaneously transmitted to the local police precinct house and to the ambulance dispatcher's desk in the regional hospital. As mentioned earlier, all calls south of 42nd Street and north of Houston Street

were referred to Bellevue. The arrangement was simple. Each of the four ambulance surgeons was assigned to a particular driver and a particular wagon. If you were put on first call during the 12-hour day period, you would be on fourth call during the corresponding night; if you were on second call during the day period, you would be on third call during the night, and you served every day and every night for one month without any time off. If the man on first call was industrious and fast while you were on fourth call, there was a reasonable chance of your not being disturbed frequently. But of this there was no guarantee. It was a matter of pride for the surgeons on first and second call to try to protect their colleagues then on third and fourth call. But it sometimes happened that all four ambulances were out at the same time.

The ambulance drivers took pride in their job and in their skill. With siren wailing and bell ringing we would dash through the snow-covered streets of New York, skidding on the turns and hoping to avoid collision. Fortunately we generally did. At the site of the call we would usually be met by a police officer who was supposed to make himself helpful to us. The typical call was on the top floor of a 5-story walk-up tenement, and up I would trudge, carrying my 40-pound satchel full of largely useless equipment. My white trousers assured uniformly courteous treatment by all classes of people whom I encountered during this month. The policeman on call was usually helpful when it came to such difficult tasks as carrying a stretcher loaded with an obese patient down four winding flights of stairs. In general, on all ambulance calls one did what one could. Sometimes the call was quite trivial. Mrs. A. had trouble getting to sleep because she was bothered with a toothache: prescription--aspirin and codeine. Then there might be another call at precisely the same address but from the adjoining apartment. When one had again trudged up the five flights of stairs, one found that Mrs. B. had noticed that the ambulance doctor had called at the home of Mrs. A. "What's the matter with her, anyway?" On other occasions the problems were serious. A possible broken back or a possible acute surgical abdomen. Sometimes the problem had already been settled, as when I was called to "pronounce" over the residue of a man who had jumped out of the top floor of a 14-story building. The appropriate notation was DOA (dead on arrival). Often the problem was a stuporous alcoholic. For these there was a special treatment. The rule at Bellevue Hospital was that if the patient was not in profound stupor, he could be

deposited at the alcohol ward where no physician was necessarily disturbed. The attendant at that ward knew better than any of us what to do with an alcoholic. On the other hand, if the patient was in a profound stupor and there was a possibility that he might have a fractured skull or be in coma from other causes, he had to be admitted to the emergency ward, which meant a complete medical workup. Particularly if the hour was late, it was a matter of pride to try to arouse the patient as the ambulance entered the gates of Bellevue Hospital. One of the ways of doing this that we soon learned was most effective was to pour the contents of a can of ether over the patient's genitals. The sudden chill might not awaken the dead but it surely aroused many who were stuporous. Furthermore, the ether quickly evaporated and left no telltale stains. When you were on first call, you rarely found time for a doughnut or a cup of coffee. When on fourth call, on the other hand, if you were lucky you might actually get some sleep. So the month went on from adventure to adventure. Occasionally there was an obstetrical problem and indeed I was called on one such case. The mother was most apologetic, stating that she had called her aunt in the Bronx to come down and take care of the delivery as Auntie had done on all prior occasions. But apparently Auntie was lost in the subway and she was very sorry but she thought that it was all over by the time I arrived. You may rest assured that it was all over. It was all over the bed, all over the floor--indeed, all over the room. I did what was necessary, ligating the umbilical cord with the small tape that was supplied and executing the birth certificate. I offered the woman hospitalization, which she declined, and recommended that she attend the postpartum clinic which I am sure she did not do. Before departing, I remember that the father offered me a drink of vino.

I remember one call to a storefront suite on East 4th or 5th Street. The suite was occupied by a family of gypsies of which we would see an occasional representative in the Bellevue population. The patient, an obese elderly woman, was lying on the floor, breathing atertorously, having apparently had a stroke. The room was poorly furnished, the major object being a stack of dirty feather beds in the middle of the room out of which at various levels heads of small gypsy children projected. There were also two young men, extremely nattily dressed, with very shiny pointed shoes and diamond stick pins in their neckties. These were the patient's two sons. When I suggested that the patient be hospitalized, the two sons objected on the grounds that a

gypsy had once died in Bellevue Hospital and it was a custom of their tribe never to return to a point at which a tribe member had died. I therefore said in that case that they would have to sign a release that hospitalization was offered and declined. This they refused to do. Here was a quandary which was further complicated by an interruption from the policeman, who pulled me aside to tell me that he believed the victim was shamming, trying to avoid arrest, and that she was wanted on a pickpocket charge in Jersey City. Wouldn't it be possible for the ambulance to pick her up, drive her through the Holland Tunnel, and deliver her to the police in Jersey City, thus avoiding the expense of extradition? I told him that I thought this was outside my duty. By this time the two sons, worried by my whispered conversation with the policeman, came forward and agreed to sign the release. As I left the room, I noted that the victim lying on the floor opened one eye and watched me depart. The patient was clearly not as comatose as she was pretending to be. If the ambulance call did not result in the bringing of a patient back to the hospital, it was customary to stop at a drugstore and telephone the dispatcher's desk to secure any new instructions. If none were forthcoming, we might then return to the waiting room at the hospital to await the next call. There were many curious problems. One of these derived from a woman school teacher who resided in an apartment at Sutton Place, which is the eastern extension of 42nd Street and therefore just within Bellevue's district. This lady was a severe heroin addict and she had discovered an ingenious way of beating the system. She would call for an ambulance and, when the ambulance doctor arrived, calmly demand a shot of morphine. If the ambulance doctor was young and naive he might refuse to give her the morphine, in which case she would quietly say, "Goodnight," and as soon as he left the apartment she would put in another call. Often the same physician would be called back to her apartment several times in rapid succession in an evening, and sooner or later he would grow tired of the game and give her the narcotic which she requested. In this way she had provided herself with the morphine that she needed at no expense to herself, because as mentioned earlier, even the telephone charge was reimbursed. But we, the ambulance doctors, were angered by this practice and finally got to Dr. Jacobs, the director of Bellevue Hospital, asking that he in some way see that this practice was stopped. This he did by rendering the unfortunate woman a bill for all of the ambulance calls, which by that time amounted to 50 or more, so that even at

the modest charge of \$10 per call the bill was significant. Abruptly the addict discontinued her practice, probably finding some other way to handle her habit.

Because of the constitutional amendment which forbids cruel and unusual punishment, known addicts when arrested on any charge, such as vagrancy, had to be supplied with their drug. When this notion got about, many drug addicts in New York, when they were in need of drugs, managed to get themselves arrested on vagrancy charges and then demanded the required drug of the station sergeant. He had no recourse but to call the Bellevue ambulance. And so it became a regular habit for the Bellevue ambulance to call at the police precinct station at 11 or 12 o'clock each night to put the addicts to sleep. I would arrive with my black bag and the officer in charge would have all the addicts lined up with their sleeves rolled up. One might have qualms as to whether this was the practice of good medicine but one really had no alternative. We were assured that it was the law. I can well remember some of these unfortunate people using their rolled up shirt sleeves as tourniquets and urging me to "Shoot it in the main line, Doc." This we had been advised not to do.

One of the duties of the Third Medical Division was to provide medical services to the Bellevue Psychiatric Hospital, and this was done by assigning each medical intern to one month of service in that institution. It was here that I had close contact with Dr. Norman Jolliffe, a distinguished nutritionist, himself a severe diabetic and a charming and cultured gentleman. It was under his surveillance that it fell to me to inject into the vein of a severely polyneuritic alcoholic the very first industrial preparation of thiamine hydrochloride in the hope of correcting a neural disease. As noted in an earlier chapter, in this case but in no other we achieved a remarkable cure. I have no explanation to offer for this apparent miracle.

Another feature of the Third Division was that it provided medical and surgical services to the prison ward, which was also located within the Psychiatric Hospital. Here one truly met the criminal class. The ward, of course, was locked and under the continual surveillance of one or more police officers. The medical and surgical problems were varied but there was one patient whose problem was memorable. This was a purported criminal who was shot by a policeman while fleeing from the scene of a crime. The bullet entered his cervical spine and produced a complete transection at the 4th

cervical level. The man was in profound coma and was totally paralyzed. This included not only his arms and his legs but also his bladder. As a result of this he required frequent catheterization and soon developed, as was almost inevitable, a cystitis and ascending pyelonephritis. This, in turn, caused him to have a high fever. Quite remarkably, however, although his temperature curve was on the upper reaches of the front page of his chart, his pulse rate remained absolutely steadily at the normal figure of about 70. Almost any situation causing a fever will also cause a tachycardia, typhoid fever being a notable exception. There was no reason to suppose that this man had typhoid fever, and the question therefore was raised: "Why did he not show a rapid pulse rate?" This question was fired at me by my visiting surgeon one morning, and the best that I could do was to venture a guess that the preganglionic fibers of the stellate ganglion had been interrupted by the bullet wound. My surgeon, Dr. Bogatko, was unimpressed by my answer and ordered me to find out about it.

Since my early days in medical school, I had always felt that every opportunity should be developed wherein the preclinical and the clinical sciences might be brought together. Across the street from Bellevue Hospital was New York University Medical School, and it had a very distinguished Department of Physiology headed by the famous renal physiologist, Homer Smith. I had not met Homer Smith at this time but I took it upon myself to telephone him and explain that we had here on the prison ward a setup for an elegant physiological experiment. We had a patient who was certainly going to die and who exhibited a curious dissociation between regulation of temperature and regulation of pulse rate. This was precisely the kind of situation that physiologists delight in generating in the laboratory. Here was a patient waiting to be used as a possible source of new and useful information. Were there any experiments which he could suggest that might be performed on this subject? Were there any drugs which might usefully be applied? I very much regret that the best answer I could get out of Homer Smith was remarkably like that of the executioner in Alice in Wonderland when ordered by the King of Hearts to decapitate the Cheshire Cat. You will recall that the Cheshire Cat had a disconcerting habit of fading away, leaving behind nothing but its grin, and this annoyed the King. He therefore shouted, "Off with its head!" This the executioner declined to do on the grounds that he had never done anything like that before and didn't intend to start in at his time of life. So spoke

the great Homer Smith, much to my chagrin and disappointment. He refused to cross the street or to send any of his faculty over to visit our interesting phenomenon. In consequence, we never did learn exactly what it was that kept our patient's pulse rate so uniform during his terminal days.

I very well recall being summoned to the admissions office of the Psychiatric Hospital to meet a young male patient who had attempted suicide. He appeared in reasonably good health and I therefore questioned him closely to learn that, yes, he had tried to kill himself. The reason for this action was that he was doing very poorly in high school and had actually failed a final examination. When I inquired into his choice of method, he told me that he had ingested a poison--namely, silver cyanide. All my earlier chemical education could not be contained and so I blurted out, "You need not tell me. I know which course you are failing. It must be chemistry!" Very angrily the patient retorted, "Yes, but how did you know?" I then explained to him that whereas most cyanides are water soluble and extremely poisonous, silver cyanide happens to be one of the few that are remarkably insoluble and therefore would be expected to be less poisonous. This may have been good chemistry, but it was obviously poor psychiatry. He turned on me with great anger and explained that it made him very, very sick, indeed.

At the end of the exhausting first year of internship I had earned two weeks of leave. My mother arranged for me to take a Caribbean cruise. I boarded the ship and slept for the next three days and nights. The boat touched at Venezuela, Havana, San Juan, and Charlotte Amalie, but except for two pretty girls I recall very little of the voyage. Most of the time I slept.

Refreshed by my vacation I returned to six months on the pathology service. During this period I performed approximately 80 autopsies, which we were trained to do by the classical Rokitansky technique. Both the gross and the microscopic studies were done with extreme thoroughness under the nominal direction of a charming if somewhat bibulous professor of pathology, Dr. Douglas Symmers. The pathology building was shared with the office of the medical examiner of the City of New York, a relatively novel institution which replaced the old-fashioned coroner's office. The medical examiners were highly professional experts in pathology and in medical jurisprudence. They spent much time as witnesses in homicide cases and were generally regarded as formidable witnesses. They had developed many fascinating tricks to establish

with precision the nature of the death of murder victims. Every spring, when the ice melted in the upper reaches of the Hudson River Valley, a number of so-called "floaters" would be pulled out of the river along the docks of Manhattan, often bound hand and foot and sometimes perforated with bullet wounds. It became a matter of considerable importance to establish whether or not these victims were alive at the time of their immersion in the river. This judgment was based upon analyses of the fluid in the right and left chambers of the heart for salt content. Any significant difference between these two analyses would argue that the individual had breathed after immersion. I also recall fascinating discussions with medical examiners on the way one distinguished between a victim who had been hanged and one who had been garroted.

I finally achieved the high level of senior house officer in medicine. By this time I had learned the whims and peculiarities of the several visiting physicians and knew how to cope with them as well as with most of the problems that rose on my wards. One of these visiting physicians was a young man generally regarded as something of a genius. This was James A. Shannon, who was at that time on the renal service. He arrived on my ward one morning, followed by a group of third or fourth year medical students, and demanded to be shown a patient with renal disease. This demand was easily met and I led him to a patient who was in profound uremic coma. In those days, of course, we had no hemodialysis and renal transplant was a procedure still in the remote future. In fact, there was very little of importance that we were able to do for patients in this condition. Shannon therefore turned upon me and said, "Dr. Stetten, do you have any thoughts as to what we might do for this man?" The reader may recall that I did serve some time in the neuropathology laboratory of the Boston City Hospital with Frank Fremont-Smith, a great authority on cerebrospinal fluid. Leaning upon information that I had gathered from Frank, I suggested that the choroid plexus resembled both in structure and in function an enormous glomerulus, which is the functional unit of the kidney. Therefore, since this man's kidneys were no longer operative, it might be useful to insert a needle into his cerebrospinal canal, draining off spinal fluid and achieving a cleansing effect by simultaneously infusing appropriate fluid into his vein. In this way, the choroid plexus might substitute for the function of the kidney. I remember that Shannon looked at me in bewilderment and finally said, "That is the craziest idea I have ever heard." To this I

could think of no response. Many years later when I served under Shannon, who had become director of the National Institutes of Health, I discovered that he still recalled this episode, which of course I shall never forget.

Upon the conclusion of my residency I sailed for Naples on one of the luxury ships of the Italian line and at the Excelsior Hotel there met my mother, who was completing a global circumnavigation. The next night we traveled by rail to Messina and thence by car to the magnificent San Domenico Hotel in Taormina. What a contrast to Bellevue Hospital! We then drove the circuit tour of Sicily. Memorable were Agrigento, Syracuse, and Palermo. From the last-named city we sailed back to Naples and after a few days of sightseeing returned to New York by boat. In January of 1937 I entered the Ph.D. program at Columbia, which was described in Chapter I.

Chapter VI

BIOCHEMISTRY AND BIOCHEMISTS

The climax of the sequence of events leading to the Ph.D. degree in biochemistry at Columbia University was the oral defense of the thesis traditionally held at that time in a room in the Low Library at 116th Street. On my committee, in addition to representatives of the Biochemistry Department of P & S, sat the redoubtable Harold Urey, the Nobel laureate who had discovered both deuterium and heavy nitrogen. The entire exercise, though somewhat frightening, proved to be less formidable than I had anticipated, Urey limiting his questions to elementary thermodynamics. As for the biochemistry faculty, their questions had been more or less anticipated. At the end of the inquisition I was asked to leave the room, and a few minutes later Rudi Schoenheimer invited me back in to be told by the chairman, Hans T. Clarke, that I had successfully passed this hazard. My dissertation was published in 1940 in the Journal of Biological Chemistry as two successive papers, and an appropriate reprint served to fill the requirement that a printed dissertation be filed with the library of Columbia University. The work that was reported in this dissertation involved the preparation of palmitic acid, the 16-carbon straight chain fatty acid, labeled with deuterium, and its administration to rats followed by the isolation of various fatty acids from the depot and liver fat of the animals. The initial preparation was not devoid of excitement. It involved the platinum-catalyzed exchange between palmitic acid and heavy water. In those days we had to make our own platinum catalyst, and at the termination of the reaction we were obligated to recover the precious platinum. There were very few research grants and one had carefully to monitor the cost of research. The preparation of the catalyst was a fascinating piece of metallurgical cookery, and the activity of the catalyst was critically dependent upon the cooking skills of the chemist. Ammonium chloroplatinate was mixed in proper proportions with a reducing agent and then heated over an open flame in a porcelain vessel called a casserole. As the color changed from orange to dark brown, one had to make a judgment of the proper moment to discontinue heating. The resultant cake was ground up under water and the insoluble platinum black was filtered off. The next step, the exchange reaction,

had to be run at high temperatures. This was achieved by sealing the three reagents--palmitic acid, heavy water, and platinum black--into a glass bomb tube, which was then laid inside a steel jacket in a bomb oven and heated to a preset temperature. Both skill and good luck were required to seal off the bomb tube in such a fashion that it would not explode during the reaction and also could readily be opened at the end of the reaction. It was at this point in my career that I determined to master the craft of glassblowing, and with due modesty I can state that I ultimately became quite proficient at this fascinating craft. In fact, I got to be so good that a few years later I was offered a position as a glassblower in the Boston shop of the supply house of Macallaster and Bicknell at a salary considerably higher than my then wage as an assistant professor in the Harvard Medical School. For many years thereafter, as my chores became less laboratory based and more administrative, I continued to be the glassblower of choice in the research section that I commanded.

The substance of my dissertation was the interconversion of fatty acids and their related derivatives, the aliphatic alcohols. The most important single finding was that the 16-carbon fatty acid, palmitic acid, was readily converted in the body of the animal into the 18-carbon fatty acid stearic acid, thus suggesting for the first time that fatty acid synthesis in the body was accomplished by 2-carbon incrementation, a sequence of events subsequently elucidated in detail by Lynen and others. In addition, I was able to show that the introduction of a double bond in the 9,10 position of the 16-carbon fatty acid also occurred in the body of the rat, yielding palmitoleic acid. It was, of course, a golden age in the era of intermediary metabolism, since isotopes had only recently been introduced and almost any experiment that one designed was likely to give important and conclusive results.

After earning my Ph.D. degree I continued on in the Biochemistry Department at the College of Physicians and Surgeons, first as instructor, then as assistant professor. The day after my oral examination I received an invitation from my former tutor at Harvard, Dr. Frank Fremont-Smith, who was by then the medical director of the Josiah Macy, Jr., Foundation, to lunch with him and discuss my future plans. I had already in mind certain metabolic interconversions that needed study. These were the interactions of those nitrogenous materials which are found in the phospholipids--namely, ethanolamine, choline, and serine. With the recent availability of N15, the possible

occurrence of such interconversions could now be determined in the intact animal. I recall discussing these matters with Frank and he suggested that I apply for a grant-in-aid from the Macy Foundation to cover the cost of a technical assistant, some equipment, and supplies. My first grant application, which was in the form of a letter, requested and secured a total of \$2,400, of which \$1,200 was the annual salary of a technician, Mr. Fred Grail, and \$1,200 was made available for the purchase of a modest (Coleman) spectrophotometer, isotopes, and other materials. Initially I continued to occupy space in the large laboratory on the 5th floor of P & S shared by all graduate students in the department, but later, having achieved the dignity of instructor, I was given a separate room.

I had significant teaching obligations and these I took very seriously. I was assigned the responsibility for lecturing on carbohydrate metabolism and diabetes, as well as on the metabolism of heme and the bile pigments. Furthermore, the entire faculty was expected to be present in the teaching laboratory during those hours when the medical students were in attendance.

I always enjoyed lecturing to students and prepared my talks with care. I recall during my first lecture on bile pigments discovering that many, or most, of the first year medical students did not know what was meant by the word "jaundice." I was the only medically trained member of the Biochemistry Department and therefore was perhaps more sensitive to the role of a biochemistry course in medical education than were most of my colleagues. It seemed to me that there would be great advantage in relating biochemistry and the other basic medical sciences to clinical problems wherever this was feasible. I discussed this matter with Dr. Franklin Hanger, who was in charge of liver disease in the Department of Medicine at P & S, and it was agreed that he would conduct a clinic for first-year students designed to introduce them to the common causes of jaundice--namely, obstruction of the biliary tract, intrinsic disease of the liver, and hemolysis. The following year, when I met the medical students to teach them about the chemistry of the porphyrins and the bile pigments, they had the basis for an interest in these compounds. They had seen jaundiced patients and had been shown the distributions of bile pigments in urine, serum, and feces in jaundices of different etiologies. Somehow the complex structures of the bile pigments became more meaningful, since it was now entirely clear that these compounds really had to do with human disease and that the understanding of these diseases was predicated upon knowledge of the

compounds, of their structures, and of their metabolic relations. It was this experience more than any other that convinced me that there might be an advantage to teaching biochemistry to fourth-year medical students who were already well aware of the nature of disease rather than to first-year medical students, and this was an educational program which I subsequently initiated.

The Department of Biochemistry at Columbia was in its heyday due largely to the skill of Hans Clarke in attracting to the department German and Austrian refugees who were pouring into this country during those years. Among these, in addition to my own preceptor, Rudolf Schoenheimer, may be listed Oskar Wintersteiner, Erwin Brandt, Karl Meyer, Erwin Chargaff, and Zacharias Dische. All of these scientists, trained in German institutions, worked for many years in the department and made great contributions. They were in some regards an odd assortment of individuals and certainly exhibited a variety of curious behavior patterns. Clarke was a remarkably tolerant chairman and managed to hold the department together with what by current standards must have been a ridiculously small budget. Weekly seminars were given either by faculty or by graduate students, and these sometimes degenerated into splendid battles. No holds were barred.

Graduate students in the department numbered about a dozen or more and included a number of young men and women who subsequently made fine careers for themselves: Samuel Gurin, William Stein, Earl Evans, Elvin Kabat, Lewis Engel, Norman Weiasman, Sarah Ratner, David Shemin, Boris Magasanik, and Konrad Bloch, not to mention Marjorie (Roloff) Stetten and myself. We shared an enormous laboratory room where there was a commonality of purpose and effort. We worked hard, late into many nights, and always all day on Saturday, but I have no doubt in retrospect that we had far more fun than do Ph.D. candidates today. We made much of the apparatus that we used and synthesized most of the compounds that we required. In general, all of us knew on a daily basis what all of the others were doing. I believe that much has been lost by the abundant modern construction that provides nearly every graduate student with a room of his own.

There was, I believe, no Federal money coming into the department. Hans Clarke had a perennial grant of about \$25,000 from the Chemical Foundation, which provided stock in our glassware room and in our chemicals stockroom. The monies dispensed by the Chemical Foundation came from funds which were collected from German patents confiscated by the U.S. Alien Property Custodian

after World War I. Rudi had a small grant from the Josiah Macy, Jr., Foundation and others of the faculty must have had small grants of their own. At that time, there was no Federal support whatsoever for such frivolous activities as biochemical research. So we fabricated, we repaired, we modified, and we made do. All in all, it was a happy--if somewhat irresponsible--era. The country was recovering from the Great Depression and heading toward World War II. The Italian-Ethiopian War and the Spanish Civil War engaged our attentions and divided the graduate student population into political factions. We were all avid readers of newspapers.

Hans Clarke wanted to provide his department with the most modern and best possible machinery. To this end he procured what may have been the first ultraviolet spectrograph housed in any biochemistry department in the United States. It was a remarkable and massive instrument, built by Adam Hilger of London, mounted upon a sturdy optical bench with a large quartz prism and a fascinating little rotating shutter called a Spekker, which permitted the attenuation of light entering the control cell. It was fired by a hydrogen discharge tube which was homemade and which exhibited a persistent spectral contamination due to mercury vapor. The record was made upon a glass plate which, because of the optics of the system, had to be pressed into a plate holder that imparted to it a slight curvature. Many were the glass plates that broke. The better part of a day was required to photograph serial spectra from which a single absorption curve could be derived.

When Dole and McInnes, at the Rockefeller Institute, constructed the first glass electrode, Hans Clarke had to have one. This was the first piece of electronic gear to enter our laboratory. It was necessarily homemade, and in order to make it, Clarke added to the department Mr. Fred Rosebury, a school dropout fascinated by radio who was earning his living as a ship's radio operator. When his ship next called at New York harbor, he was persuaded by his brother, a microbiologist in the Dental School at P & S, to give up radio and become instead one of the first electronic technicians in a biochemistry department. His initial assignment was to reproduce the instrument of Dole and McInnis, which he successfully did. He subsequently designed and built a device for reading the spectrographic plates that were generated by the Adam Hilger instrument. It was, I believe, our unique ability to do ultraviolet spectra of organic compounds that attracted Oskar Wintersteiner, our steroid chemist, to P & S.

Fred Rosebury was an expert operator of the turret lathe and was thoroughly familiar with the electronics of that era. He modified and improved the measuring circuitry of the glass electrode and designed and constructed a variety of electrical and mechanical instruments for all of us. Thus he built the exquisitely precise automatic pipette which delivered the drops of water into the falling-drop apparatus used for the measurement of deuterium oxide. He also had a major role in the construction of our first mass spectrometer, a machine of the Dempster pattern. The internal parts had been fabricated for us by Harold Urey's technician, but all of the accessory parts--and these filled a room--were constructed at P & S. I well recall the excitement of making the great magnet, which was wrapped with insulated copper tubing that served as the electrical conduit. It also served to contain the cooling water which had to be circulated continuously through it. The actual procedure took place on a large lathe and the relatively stiff tubing was fed, layer by layer, onto the spool, with several of us hanging on to make appropriate tension and get the windings as uniform as possible. The several layers were then connected in series for the electrical flow and in parallel for the water flow. Large regulated power supplies being at that time not available, a vast array of automobile storage batteries was employed to hang in the DC circuit which activated this magnet. The final reading of the mass spectrometer employed a d'Arsonval galvanometer which was exquisitely vibration sensitive. It was therefore hung from a "Julius suspension," a piece of piano wire hanging from a ring bolt in the ceiling, to which was attached a heavy construction including two Ford flywheels fastened together with the tie-rods and bottomed off with copper veins which were immersed in a pan of oil to dampen any oscillations. Miraculously, the Julius suspension exceeded our expectations and provided a very stable platform for the galvanometer. It befell to me, as the carpenter of the group, to make a wooden housing to protect the entire assembly from drafts. A spotlight cast a beam onto the small mirror of the galvanometer, which was in turn reflected on a long ground-glass scale, thus amplifying deflections. The instrument was used as a null-point indicator, the potential generated at the collecting electrode of the mass spectrometer being offset by the output of a Leeds and Northrup potentiometer. By modern standards the instrument was certainly very primitive, but in its life it probably generated more important isotope analyses than has any other instrument since that time. I was proud to have had a hand in its construction.

Fred Rosebury, in addition, had many extracurricular interests. He was an excellent photographer and also a fine amateur painter. This latter hobby I always suspected was selected out of perversity because he was totally red-green color blind. He simply could not discriminate between these two hues, both appearing dull gray to him. When he painted, therefore, it was necessary that he be accompanied by his adoring wife, Pauline, who would from time to time suggest the use of a red or green pigment. Fred's painting was unschooled but nonetheless arresting and I am happy to possess two of his works. He was, in addition, an excellent performer on the guitar, favoring what today would be called country-style music. Though relatively lacking in formal schooling, he was one of the best-read men I have known and was continuously taking correspondence school courses in all and sundry subjects. He finally was recruited by Jerrold Zacharias at the beginning of World War II to join a group at MIT devoted to the development of submarine detection by sonar. While there he developed material which ultimately led to a course on the design and construction of vacuum tubed, about which he published a textbook. It was a deep source of gratification to his many friends that Fred Rosebury, who never graduated from high school, appeared on the roster of the faculty of MIT with a course of his own.

Sometime later, when I moved from Harvard to the Public Health Research Institute of the City of New York, I took with me another gifted electrical and mechanical technician, Frank Rennie. In preparation for his work he had at various times been employed as a maker of dental prostheses, as a jewelry manufacturer, as a worker in a boiler factory, as a designer and installer of radio equipment in a fleet of police cars, and in various other crafts. There were few tools with which Frank Rennie was not totally familiar, yet he continued to take courses in this area all of the time that he was employed at the Public Health Research Institute. He delighted in working at micrometer precision and was always willing and ready to be of assistance to any of the laboratory workers who needed his talents. I have always held persons of this sort in particularly high esteem and regret the relative scarcity of such individuals in our current biomedical research effort.

The earliest recollection I have of biochemists goes back to my childhood when my parents entertained Phoebus Aaron Levene as an occasional guest in our home. He was the brother of our family dentist but, what was more important, he was one of the original members assembled by Simon Flexner at the time of

formation of the Rockefeller Institute early in the century. He was trained, of all places, in the St. Petersburg (Russia) Military Academy and boasted of being the only biochemist ever to have risen in that stern environment. He was one of the leaders in the United States in the study of sugar chemistry, and is chiefly remembered for having identified the characteristic sugars of so-called thymus nucleic acid (2-deoxyribose) and of yeast nucleic acid (ribose). He devoted much effort to an attempt to provide structures for these two nucleic acids but the results were entirely erroneous. He adhered to the view that the nucleic acids were actually tetramers of nucleotides containing one mole of each of the four constituent nitrogenous bases. He was responsible for studies attempting to assign absolute configuration to sugars of various rotatory power and he was fascinated with the phenomenon of mutarotation. P. A. Levene was a wispy, frail little man with a sallow complexion and white hair, which he wore long. In private life he was a successful collector of French Impressionist paintings. On a few occasions, I, as a high school or college student, visited his laboratories in the Rockefeller Institute facing the East River at about 68th Street.

A member of the Columbia Department of Biochemistry whom I came to know very well was Oskar Wintersteiner. He had secured his doctorate in Austria at the University of Graz under Fritz Pregl. Pregl had devised the methods of organic microanalysis upon which an era of organic chemistry was critically dependent, and Oskar was, I believe, the very first student from Pregl's laboratory to come to this country. He was brought here by the pharmacologist at Johns Hopkins, Professor J. J. Abel, for the specific purpose of performing analytical studies upon an early preparation of crystalline insulin. After measuring the remarkably high content of sulphur in this protein, Oskar moved on to the Rockefeller Institute where he was retained by Karl Landsteiner, one of the fathers of immunochemistry and the discoverer of the major blood groups in man. He set up an organic microanalysis laboratory at the Rockefeller Institute and subsequently was brought by Hans Clarke to P & S where he again established a laboratory of microanalysis. He retained as a technical assistant Willie Saschek, a blond, rosy-cheeked, rotund little man who had all of the compulsive fastidiousness that was required of a microanalyst. Two of his personal habits will reveal this. It was his practice to measure the pressure in each of the tires of his car every day and to plot these data, thus permitting him to forecast when air would be required in each of the tires. Also,

when he ordered coffee with cream at the local drugstore, he would pour the cream into the coffee and then carefully rinse out the little cream jug with successive spoonfuls of coffee in order to effect a "quantitative transfer." Such a person could be relied upon to extract maximum precision out of the analytical methods that were then in vogue. These depended chiefly upon a very sensitive instrument, a Bunge or a Ruhlman microbalance. Each graduate student in the Department of Biochemistry was required to take the course of instruction in microanalysis which was given chiefly by Willie Saschek who was a very demanding taskmaster. Because one was working at the very limits of available precision, one had to exercise extraordinary care in every manipulation. The climax of the course was the performance of satisfactory analyses on a series of "unknown" compounds under the watchful eyes of Saschek and Wintersteiner. Oskar was at this time a bachelor and an enthusiastic musician. I lived at home with my mother, who was also very much interested in the piano, and we had a fine Steinway baby grand which Oskar liked to play. He was therefore a fairly frequent visitor, a tall and distinguished-looking man with a taste for skiing, which was a residue of his earlier Austrian background. He was the pianist to the Rosebuds, a chamber music group which also included Joe Victor, a pathologist, and Sam Gurin, G. L. Foster, and Robert Herbst--all biochemists. There were other occasional affiliates to the Rosebuds and, indeed, when they chose to play the Toy Symphony, I was given the part of the cuckoo which I performed on the ocarina. The most memorable performance of this group, and they were truly not very good, was the Schumann Forellen (Trout) Quintet, which they performed with gusto and enthusiasm.

Oskar's research interests, as I recall them, were initially in the field of steroid chemistry. He was particularly interested in the increasing numbers of steroids that were being isolated from the adrenal cortex, for several of which he provided structures. He was a meticulous organic chemist and devised many of the methods of organic micromanipulation which have since become standard practice. Ultimately, Oskar fell in love and married a tall and beautiful technician who worked with Joe Victor. We encountered Oskar and Peggy and their two children much later in life after Oskar had left Columbia to become chief of chemical research at Squibb, with headquarters in New Brunswick, New Jersey. When Marney and I moved to Rutgers Medical School, we again saw much of the Wintersteiners until Peggy's death and Oskar's return to Graz.

The contemporary biochemist with whom I had closest association was probably Lewis L. Engel. He and I had resided in Matthew Hall during our senior year at Harvard and had crammed together for our divisional examination in biochemical sciences before graduation. He had moved into the Columbia Biochemistry Department as a Ph.D. candidate simultaneously with my entrance into the medical school and we continued to see a great deal of each other. Lew was a nephew of the great diagnostician of Mount Sinai Hospital in New York, Dr. Emmanuel Libman, one of the most accomplished physicians of his time. Libman is famous as the first to describe the disease subacute bacterial endocarditis, which was an important cause of death--particularly to the victims of rheumatic fever--in those days before antibiotics. His home and office were located on East 67th Street, not very far from my family's home on Park Avenue at East 77th Street. Lew, his widowed mother, and his identical twin younger brothers, George and Frank, all lived in Libman's home where Mrs. Engel kept house for her bachelor brother. Libman was something of an eccentric. He had an enormous collection of phonograph records and the phonograph was continuously playing. Lew and I in those days shared an interest in photography and constructed a modest darkroom in Dr. Libman's house.

Lew was a wit and a prankster. Many of the comic events that occurred in the great graduate student teaching laboratory at P & S were of his construction. It was Lew who discovered that if a Bunsen burner was fastened to the water spigot rather than the gas line, it became a weapon of considerable effectiveness, resembling a continuously firing water pistol. It was he also who made the observation that if one took a mouthful of glass beads and an appropriately sized glass tube, one could, blowgun fashion, pepper the enemy with beads. If the glass beads were bounced off a window, a noise was generated that sounded remarkably like a piece of chemical apparatus undergoing fracture. This particular device was used with great effect to harass a fellow student, Doris Blumenthal, who was kept in a continuous state of anxiety believing that cracks were springing up in her rather elaborate, all-glass extraction apparatus. When she finally discovered the source of her trouble, Doris, an imposing and muscular woman, picked up Lew, who was on the small side, and totally immersed him in one of the large laboratory sinks. All of the colleagues were vastly entertained by this display. Lew also made it a habit to collect cracked or partially broken glassware. He would then walk up behind someone who was busily engaged in a chemical experiment, concealing a

cracked beaker behind his back. At the appropriate moment he would permit this to fall to the floor with a resounding crash. During the International Physiological Congress in Rome, Lew, without cracking a smile, advised a naive colleague that he must certainly visit the Cinquicento; and furthermore, when there, seek out an old friend, Al Fresco, who would show him around. All in all, Lew, who himself was a very astute biochemist, maintained among the Ph.D. candidates a spirit of frivolity which I believe is largely lacking in this population today. Upon completion of his Ph.D. studies, he went to Switzerland to study terpene and steroid chemistry with Ruzicka. He ultimately returned to Harvard where he served first at the Massachusetts General Hospital and then in the new Institute of Reproductive Biology, finally taking his rotation as chairman of the Medical School Department of Physiological Chemistry. In the later years I saw relatively little of Lew, though we always maintained contact.

Lew was twice married. I served as best man on the occasion of the first wedding, which was conducted in the apartment of the bride's family and was in the Jewish tradition. At one point in the ceremony it was necessary for the bride and groom to drink wine from a common glass and then smash the glass. When the mother of the bride realized what was about to happen to a piece of her best stemware, she quickly substituted a kitchen tumbler, but this vessel merely bounced when it was thrown on the ground. Lew rose to the occasion. As an old laboratory hand he knew exactly what to do. He called for a towel and for a hammer. He wrapped the glass in the towel and successfully smashed it with the hammer, thus completing the marriage ceremony. As best man, it was my job to drive the bride and groom to the pier from which they were to sail on a Caribbean honeymoon. On the way down, Lew commented to me that he intended to have a very good time. I told him that I was sure he would, but was somewhat startled when he explained to me that the reason for his cheerfulness was that he had in his satchel a copy fresh off the press of a new textbook of physical chemistry by Debye and Huckel. My heart sank, and I correctly gave this marriage a poor prognosis. Shortly after the bride and groom returned, I was invited to their home for supper. The bride was a portrait painter, fond of doing studies from the nude. When I entered their newly furnished living quarters, I was startled to find over the fireplace a life-sized nude figure, a self-portrait of my hostess. It was remarkably difficult for me to keep my eyes averted during the long evening.

It was during my stay at P & S that I had my first graduate student. This was George Boxer, a war refugee from Vienna who came to the United States by way of England. While in England he had served as a technician in the famous Cambridge laboratory of Sir Frederick Gowland Hopkins. George and I worked together and produced some interesting papers dealing with the nature of the metabolic defect in the diabetic rat. These studies were made possible by the then novel discovery that alloxan quite specifically damaged the beta cells of the Islets of Langerhans, thus producing a permanent diabetic state. Using isotope techniques, we were able to demonstrate that during diabetes, if unregulated, the synthesis of new molecules of fatty acid virtually comes to a standstill. The administration of insulin, however, rapidly restores this process to normal. This was a major defect in the disease which had previously escaped notice. After leaving Columbia, George joined the research staff of Merck in Rahway, New Jersey, where he remained during the rest of his life. By the time I got to Rutgers Medical School, George had achieved a high position in the Merck Sharp & Dohme Research Laboratories. It was during that period of time that George developed carcinoma of the lung and subsequently died with a brain metastasis. His friends, and particularly his colleagues at Merck, raised a substantial amount of money to endow a permanent lectureship in his memory at Rutgers Medical School. His wife, Lily, accompanied often by one of his two sons, makes it a practice to attend these lectures.

Another graduate student of this period was William Goldwater, who also earned his Ph.D. degree at Columbia under my preceptorship. Our paths crossed again when I came to the National Institutes of Health where Bill has made a position for himself in administration. He is now one of the local experts on contract-supported research at NIH. The smallness of the universe in which we circulated is demonstrated by the frequency of recurrent encounters with familiar people in new environments. Adele Karp, who came from Canada, also earned her doctorate under my guidance. She married Boris Magasanik, a fellow graduate student, and subsequently moved with him to Boston where he became a professor at the Massachusetts Institute of Technology.

An interesting association was established when Juan Salcedo arrived in New York City from the Philippines to learn something of modern biochemistry. Juan was a professor of biochemistry at the University of Manila, sent here on a minuscule scholarship. He was a man of great charm and grace and exquisite manipulative skill. Furthermore, he had remarkable patience and soon became

the man whose deuterium analyses showed the highest reproducibility. He would persevere in the process of timing the free fall of drops of water over and over again until the results secured were satisfactorily precise. With me, Juan studied the nature of the lipid defect in obesity.

His entire family--wife, five children, brothers, parents, etc.--was left behind in the Philippines, and in 1941 his homeland was invaded by the Japanese. He lost all contact with his family and in a sense was isolated in New York. He made contact with the Philippine community in New York, instituting classes for the children of Philippine-Americans so that they might continue to learn the language, Tagalog, and to retain important elements of their island's history. Then one day Juan told me that he would not be in the laboratory tomorrow, nor even the next day, but he could not reveal why. I subsequently learned that he had been recruited to join General MacArthur in the liberation of the Philippines by the United States Army, serving, as I understand it, as interpreter and courier. He located his entire family and brought them all together. Although most homes in Manila had been wrecked by the war, his was one of the few that survived. Some months after his departure, Marney and I received a letter from him telling us that none of his children had any shoes and that no shoes were available in Manila. Apparently a ruler or tape-measure was also hard to find in Manila, so Juan included in the letter strips of paper, each torn off at the foot length of a different child. Barney and I made the necessary match in the local shoe store and sent five pairs of sneakers to the Philippines where they were received with pleasure. Juan later had a distinguished career successively as minister of health, president of the University of the Philippines at Manila, and president of their National Academy of Sciences. I continued to hear from him from time to time when visitors came to the United States from the Philippines and he visited on several occasions. He achieved his greatest distinction when he cleared Bataan Province of beriberi, the very devastating condition brought about by vitamin B1 deficiency. The natives, it turned out, were totally unwilling to supplement their diets with pills and were also unwilling to forego their traditional and very sanitary but nutritionally devastating practice of boiling rice in many changes of hot water. Juan arranged to have fabricated small capsules of thiamine which were identical in size and shape to a rice grain. These pills, suitably coated, were mixed in appropriate proportions with the rice that was marketed in Bataan Province, and miraculously the epidemic of

beriberi, which was killing many natives, subsided. This work, incidentally, was supported by Williams and Waterman who had been the original employers of my old friend, Samuel Gurin, when he was giving assistance to them in their initial preparation of thiamine.

In the course of my drifting in and out of biochemistry laboratories in those days, I of course encountered many of the prominent figures in this field. These encounters came about in various ways. Shortly after World War II, the great Hungarian biochemist, Albert Szent-Gyorgyi, accompanied by a large number of Hungarian colleagues, was brought to this country. He had been hiding out during the war in the Embassy of Sweden at Budapest. The basis for issuing passports was that he and his associates would provide teaching skills in this country. Most of his fellow Hungarians spoke little or no English. He had, however, an admirer and good friend, Dr. Stephen Rath, a manufacturing pharmaceutical chemist also from Hungary, who provided funds for the support of these refugees. It soon became apparent that the State Department would inquire into the nonexistent teaching activities of these purported teachers. In 1948, I was approached with the suggestion that I organize a course in the New School for Social Research, East 8th Street, New York, which would provide some evidence that Szent-Gyorgyi and his friends were indeed teaching. I therefore rounded up a number of prominent biologists and biochemists, including Ernst Mayr of the American Museum of Natural History, Otto Meyerhof who had come from Germany to the University of Pennsylvania, Michael Heidelberger of Columbia University, and others, to participate in a course with Albert Szent-Gyorgyi. The lectures were given on Tuesday evenings to a group of interested lay persons, who I think derived very little benefit from most of them. It was my job to make sure that the lecturer arrived on time and to provide an introduction.

One of the persons whom I came to know in this relationship was Otto Loewi, the discoverer of "Vagusstoffe" which proved to be acetylcholine. Otto Loewi, like Szent-Gyorgyi and Meyerhof, was a Nobel laureate. In addition, he was a most remarkable old gentleman. A refugee from Austria, where he had taught at the University of Graz, he was now working in laboratories provided for him at New York University. Though well on in years, he took the trouble to become an American citizen. I recall the celebration at the home of Rudi's cousin, Bill Schoenheimer, which followed his citizenship ceremonies. He came into the room with a great smile and announced, "Now I can stop saying what is

wrong with you American scientists and start saying what is wrong with us American scientists." He is also the source of one of my favorite definitions --namely, that of teleology. Loewi defined teleology as a woman with whom all men of science secretly consort but with whom they do not like to be caught in public. I have been interested to note that contemporary scientists, with increasing frequency, are willing to evoke teleological explanations before their colleagues without embarrassment. Loewi lived to a ripe old age and spent the summers of his latter years at Woods Hole, where we would see him frequently. He was known to all and sundry as Onkel Otto and was always ready to explain the basis of his fame to anyone who would listen: "Did I ever tell you how I got the idea for my Nobel Prize? I awoke one night from a deep dream, knowing precisely the experiment which I must perform on a frog. The following morning I found that I recalled having had a brilliant idea but was totally unable to remember what the idea was. So that night I placed a pad and pencil next to my bed and, when the dream recurred, I quickly wrote it down. The next morning I took the pad with me to the laboratory and performed the crucial experiment." I have heard this account many times but cannot attest to its absolute accuracy.

I remained a member of the Biochemistry Department of P & S until 1947. My research interests in those years centered particularly about the interconversions of ethanolamine, choline, betaine, glycine, and aerine. I also visualized the use of isotopes in the measurements of changes in rates of metabolic reactions in disease. Over the years I have explored not only diabetes but also fatty liver, obesity, muscular dystrophy, and especially gout in this way. In addition to participating in the teaching program of the Biochemistry Department, I also became involved in the teaching of the Department of Medicine. It happened in this fashion. As mentioned somewhat earlier, I became impressed with the desirability of instructing fourth-year medical students in certain aspects of biochemistry that clearly related to medical problems. I proposed that a lecture course be given in this area, a proposal which the chairman of biochemistry, Dr. Clarke, ridiculed. I therefore discussed the matter with the most active member of the Department of Medicine, Dr. Robert F. Loeb. He was the son of the great Jacques Loeb, one of the founders of modern biology, an early student of protein chemistry, and also an innovator in behavioral science. I had been familiar with the writings of Jacques Loeb since my college days and was enormously impressed with his brilliant physician

son. Bob Loeb, who was himself more interested in biochemistry than most physicians, saw at once what I was trying to achieve and indicated that he and his department would sponsor my new course offering. They gave me the use of an amphitheatre during one of the poorest hours in the week--namely, 5 to 6 on Friday afternoons. The course of lectures was started and soon attracted attention. Whereas the offering was made as an elective in the fourth-year, third year students, interns, residents, and some of the visiting staff made it a habit to attend. I found myself speaking to full houses. Because no suitable text of my subject was available, I prepared extensive mimeographed material so that the auditors were under no obligation to take notes on my talks. It was something of a shock for me to discover many years later that some of the auditors had carefully preserved these primitive and now completely outdated notes. I discussed with the students such topics as the biochemistry of diabetes, the biochemistry of jaundice, steroid and bile acid metabolism, roles of vitamins which were in those years becoming recognized as components of coenzymes, and similar topics. I personally derived enormous satisfaction from this course, which was conceptually my own creation. When, in 1947, I was invited to move to Harvard Medical School, I moved this course with me and made the same offering at Harvard. Over succeeding years, I encountered students who had attended these lectures and who told me on occasion that these presentations in the late 1940s were career-determining for them. I do not deny deriving deep satisfaction in having contributed to the career selection of, among others, Gordon M. Tomkins. My duties at P & S included instruction in biochemistry to the School of Nursing, a rather foolish exercise before a group of charming young women who had no interest whatsoever in the subject that I had to present. I tried to reduce the matter to practical issues. I recall that my big moment in the nursing course was a demonstration of what happens to a glowing cigarette when immersed in a vessel of oxygen gas. The mild explosion that ensued was supposed to alert the students to the dangers of cigarette smoking on a service where oxygen tents were in use. Whether the message actually got across or not, I do not know. During these years the School of Nursing assigned an assistant to me to take attendance, to help correct quizzes, and to perform other functions. This was Miss Elizabeth Gill, R.N., a splendid person, a descendant of Priscilla and John Alden, and subsequently dean of the School of Nursing. I recall discussing with her the striking absence of any black students in the School of Nursing at that time and learned

to my surprise the reason why none was being admitted. I was told that the student nurses all lived in a single dormitory and shared, as was common in dormitories, their shower facilities. The then dean of Nursing apparently feared that under these circumstances the color might run and for this reason she made it impossible for black students to secure admission. I have subsequently noticed that one of the last facilities to be integrated in a typical community is the swimming pool or the bathing beach, perhaps for similar reasons.

In 1947 I was visited by Professor A. Baird Hastings of the Department of Physiological Chemistry, Harvard Medical School, who invited me to join his department and the newly established biophysics laboratory. This laboratory, which was funded out of a grant from the Office of Naval Research, was to have three assistant professors, one from the Department of Physiological Chemistry, one from the Department of Physical Chemistry, and one from the Department of Medicine. My colleagues were to be Arthur K. Solomon and Seymour Gray, and we were given a series of laboratories on the ground floor of Building D in the classical courtyard of Harvard Medical School. The offer tempted me, as indeed many other Harvard graduates have been tempted back to their alma mater. Another incentive to leave Columbia was the sharp decline in morale in the Biochemistry Department following the untimely death of Schoenheimer. David Rittenberg, who had served Schoenheimer well as an analyst but lacked Schoenheimer's broad biological perspective, presumed to dominate all isotope research at P & S. It became increasingly difficult for me to obtain needed isotope analyses. In this and in other ways he managed to make my continued life in the Biochemistry Department at P & S unpleasant. I therefore looked with favor on the prospect of moving to Harvard.

My annual salary jumped upward from \$3,600 (plus \$400 for teaching the nurses) to \$5,000, and a research associate position was to be found for Marney in the same laboratory. A large-scale operation was proposed which would involve the use of stable and radioactive isotopes, and a mass spectrometer was under construction under the guidance of Solomon. This was a tool upon which my research plans were critically dependent. It should be recalled that in those days if you needed a mass spectrometer or, for that matter, a Geiger-Mueller tube, you had to build it yourself. There was no commercial source, although the tube for this mass spectrometer had been assembled for Harvard by Professor A. O. Nier of the University of Minnesota. Marney and I left our

delightful cottage in Fieldston, Riverdale, in the Bronx, New York, and found a handsome brick house on Beacon Street, Chestnut Hill, right on the Boston-Newton town line overlooking the reservoir. Here we moved in and soon acquired one of a series of loyal domestics, Mrs. Sweet, a down East Maine Yankee, who had served in various distinguished homes in the Boston area. She took over the care of our two small daughters and also of Marney and me and lived with us for many years in Boston, New York, and Bethesda. Mrs. Sweet had had 10 children of her own and there was no crisis, no catastrophe, which she had not previously encountered.

Chapter VII

HARVARD REVISITED

In February of 1941, Marney and I were married. Our wedding was a simple affair conducted at my mother's apartment by Judge Sam Rosenman, a law partner and speech writer for Franklin Delano Roosevelt. We had taken a short honeymoon to Williamsburg, Virginia, and then both returned to our respective teaching assignments -- Marney in the Biochemistry Department of the Dental School at Columbia, and I in the corresponding department of the Medical School. She was at that time working on the experiments that led to her Ph.D. dissertation under the preceptorship of Rudolf Schoenheimer. Her problem related to the biological interconversions of the five carbon amino acids, glutamic acid, ornithine, proline, and hydroxyproline, studied using stable isotopic tracers. Some years later she demonstrated for the first time that whereas proline, like all other amino acids studied to date, readily enters the proteins of the body of the rat, hydroxyproline when administered is not so incorporated. In fact, her analyses made it clear that the hydroxyproline that occurs in certain proteins, particularly in collagen, enters polypeptide linkage as proline and is subsequently hydroxylated. After gaining her Ph.D. from Columbia University, she accepted a position with a fellow biochemist and physician, Dr. Charles Fox, who was pursuing a product that accumulated in cultures of bacteria which were inhibited by sulfonamides. Marney succeeded in isolating and purifying this product and determining many of its characteristics. The product ultimately turned out to be aminoimidazole carboxamide, though it remained for others to assign this structure to the compound. The compound was of considerable interest since it was the first clearly identified product on the pathway of purine biosynthesis.

We had originally lived for a few months in my mother's apartment while our apartment building near P & S was being completed, and in the summer of 1941 we took a leisurely driving trip across country to California. On returning we moved into a brand new apartment on 158th Street and Riverside Drive where we remained until the day before the birth of our first daughter, Gail, in 1944. It was in the process of getting settled in our home in Riverdale, Bronx, that Marney's labor commenced. We were in the process of centering the living room

rug, and it was as much the anxiety of our moving man as anything else that got us into the car and on our way to Doctor's Hospital. A couple of years later our second daughter, Nancy, was born. In these and subsequent obstetrical situations, it was Marney's habit to take off approximately two weeks before returning to the laboratory. We were thus totally dependent upon live-in, full-time maid service and this we continued until relatively recently.

Prior to my move to Boston, I commuted between Boston and New York on a number of occasions, always stopping with Baird and Margaret Hastings in their charming home on Pill Hill in Brookline--so nicknamed because of the high concentration of physicians in the area. Baird was an unusual person. He had spent a number of years at the Rockefeller Institute working in the laboratory of Donald Van Slyke, an important innovator of analytical methods and a thoughtful student of blood gases and other inorganic metabolites. He had then moved to the University of Chicago before accepting the chairmanship of physiological chemistry at Harvard Medical School. Neither he nor Margaret ever learned to drive a car, and they were therefore always dependent upon their friends for transportation. He personally was very much interested in the structure of the mineral component of bone, which he had characterized as hydroxyapatite. He was a conscientious although very nervous lecturer, devoting many hours to the preparation of each lecture that he gave to the medical students. Toward me he always was a friendly and remarkably modest supervisor, never entering into my own research plans or laboratory activities. He was in general supportive.

My time at Harvard was fairly frustrating. This was due chiefly to the fact that whereas the services of a mass spectrometer had been promised to me, the mass spectrometer was, during my stay, rarely in operating condition. The matter was unfortunately completely outside my control since Arthur Solomon, the representative of the Department of Physical Chemistry in the biophysics laboratory, had full responsibility for this phase of the instrumentation. He was supported in this effort by a graduate student, Sydney Soloway, and a gifted technician, Frank Rennie, both of whom I stole from Harvard when I departed. Despite their best efforts, however, they seemed unable to maintain the mass spectrometer, which limited severely the number of isotope analyses that I could procure. Nonetheless, I initiated a research program originally in collaboration with Peter Forshan, then resident at the Peter Bent Brigham Hospital, and my valued assistant, Jean Benedict. This was a study of the

nature, distribution, and turnover of uric acid in the normal and in the gouty individual. We secured the services of an invaluable experimental subject, Angelo Lippi, known as the goutiest man in Boston, whose record at the Peter Bent Brigham was very long. We discovered, to our amusement, that his first admission had been under the diagnosis of arthritis and was signed by none other than Harvey Cushing. He subsequently became the maitre d'hotel at the Hotel Brunswick in Boston where his duties had to do with the preparation of canapes for the daily tea dance. His diet, as far as we could ascertain, was predominantly goose liver, caviar, and sardines. Perhaps partly as a result of this diet, he had acquired by all odds the largest and most imposing tophi we had ever seen, great concretions of sodium urate around his knees, elbows, and other joints. We studied this man exhaustively, mostly by administering isotopically labeled uric acid, which we had synthesized, and measuring the isotope abundance in the excreted products. We also studied tophi which had been surgically excised. All these studies led to the definition of a novel quantity, the miscible pool of uric acid, that quantity of uric acid which is in the body in a condition available to mix with intravenously administered uric acid. This quantity was consistently enormously increased over normal in the victims of gout. From these and subsequent studies, we concluded that the preponderant metabolic defect in gout was an exaggeration in the rate of synthesis of uric acid, a finding entirely consonant with more recent and more searching observations. My interest in gout continued throughout the subsequent years at the Public Health Research Institute, where Jean Benedict accompanied me when we left Boston. Peter Forsham, our early clinical collaborator, I continue to see from time to time. He now works in the San Francisco area where he serves as professor of medicine at UCSF, with a specialty in diabetes--a disease with which he has lived remarkably successfully throughout all of his adult life.

One of the real pleasures of my stay at Harvard was my association with the Peter Bent Brigham Hospital, which is situated directly across Shattuck Street from Harvard Medical School. Architecturally the Brigham was a monstrosity. It had been built many years earlier on the assumption that the best thing to do with patients was to wheel them out into sunny courtyards, a typical architect's conception that never materialized. The long and drafty corridors had gradually become cluttered with all sorts of hospital equipment for which there was a dearth of storage space. The entire building had a shoddy and rundown

appearance, but this belied the quality of medical and surgical care available. The morale at the Brigham was remarkably high. The residents and interns were extraordinarily bright, industrious, and dedicated, and the same could be said about the nursing and other services. The Department of Medicine was dominated by George Thorne. I do not recall his chronological age at that time but George was surely the youngest looking Professor of Medicine in the country. I might add that he retained his youthful appearance throughout the years that I knew him. He was particularly interested in endocrinology, specifically in diseases of the adrenal cortex, and he had assembled an alert Department of Medicine. When I arrived on the scene he promptly extended to me the courtesy of his hospital. This meant chiefly that I could dine in the doctors' dining room, a very important privilege since there was a dearth of dining facilities in the neighborhood of the medical school. I frequently availed myself of this privilege. In addition, and perhaps by way of repayment, it was my privilege to meet with the interns and residents in order to update them in biochemical matters. They were a remarkably bright bunch. Many years later, George Thorne invited me, as was his custom, to assume the position of physician in residence at the Brigham for two days. The terms of this appointment were that I should reside in the hospital occupying the chief resident's bedroom, that I should eat all my meals with the interns and residents, and that I should not tell any of my friends in Boston that I was in town. I was to be at the disposal of the residents and interns 24 hours a day for my two days of tenure. Meanwhile George Thorne himself left town and went on a vacation.

It was an awesome experience. Here for the first time in many years I had to go on rounds on a ward service --indeed had to conduct the rounds. I was, of course, ably supported by the chief resident and his staff. Nonetheless, I felt very responsible and not a little bit frightened. I had to fill out the hours by giving talks to the interns and residents on matters of common interest, and in the evening I had to be available to answer their innumerable questions. After we tired of discussing scientific and medical matters, there were still the questions of career selection. Because this was the Brigham and because the medical school across the way was Harvard, it was altogether accepted that every resident at the Brigham should, in the course of his residency, publish the fruits of a piece of research, and that preferably this should be published in a Journal of basic science, such as the Journal of

Biological Chemistry or the American Journal of Physiology. The interns and residents felt under some compulsion to meet this condition, even though many of them really aimed at becoming practicing physicians. Here was displayed for me the schizophrenia that I have so frequently encountered among persons trained in medicine and placed in a research environment, struggling to resolve the competing ambitions of medical practice and medical research. This dualism exists among the younger staff in every major teaching hospital but probably nowhere more strikingly than at the Brigham. I have, of course, encountered this same type of double loyalty in the halls of the National Institutes of Health. My loyalty to the Brigham was reactivated when many years later my oldest daughter was a patient at that hospital for many weeks. Again I had the privilege of seeing this extraordinarily fine institution functioning well under stress, and again I was reassured that the quality of medicine practiced bears remarkably little relation to the level of elegance of the building in which the practice is housed. Now the Brigham has moved into an elegant high-rise building. I hope that in the process it does not lose the extraordinary qualities that it has acquired over the past many years.

As mentioned earlier, the biophysics laboratory at Harvard Medical School was supported by a grant from the Office of Naval Research. In fulfillment of his duties, the commandant of the Naval area, which centered in the city of Boston, felt impelled to visit our laboratory presumably to report to headquarters on our activities. Baird Hastings was very nervous about this impending visit and urged us to make serious preparations. Each of us made an appropriate presentation to the captain (or was he an admiral?) when he finally arrived. He was polite but obviously totally disinterested in what we had to tell him, which had to do with the metabolism of hydroxyproline, the nature of obesity in the rat, and the design and construction of mass spectrometers. He did perk up somewhat when we asked if it would be possible to rebudget funds from the equipment budget to the payroll budget to permit us to add a secretary to the staff. At this he looked up briskly and asked, "It's all for the flag, isn't it?" We nodded vigorously and allowed that yes, it certainly was all for the flag. Approval was immediately forthcoming.

The Navy, at the end of World War II, had unexpended residues of research money which, under the influence of Vannevar Bush, were being invested in projects such as ours. When the National Science Foundation was created and the National Institutes of Health expanded its grants program in the years

immediately following, this need for Naval funds evaporated. This action by the Navy provided some continuity to the federally supported biomedical research effort that had been initiated during the war years.

After extensive reconstruction of the space assigned to us, our laboratories were ready for dedication. On this occasion we had a visit from the Board of Overseers of Harvard University which included, among other famous persons, Senator Leverett Saltonstall. It was of interest to me that all the members of the Board showed up for this relatively trivial function and all seemed to take a real interest in our progress. Certainly some of the strength in Harvard resides in the loyalty of its governing and administrative officers. That the Senator from Massachusetts should make a special trip from Washington to Boston in order to inspect the biophysics laboratory of Harvard Medical School was to me quite remarkable.

Harvard is indeed an extraordinary institution. Marney and I well remember the occasion of the first seminar that we attended in the Department of Physiological Chemistry. We had been used to the very combative and lusty seminars of the Biochemistry Department at the College of Physicians and Surgeons, and were therefore struck by the decorous nature of the presentation which was made by one of the graduate students in Hastings' department. The paper, which he had either selected or had assigned to him to report upon, dealt, if I recall correctly, with the presence of polyphosphates in blood, a matter upon which there was considerable prior literature. The present work, however, came from one of the many laboratories associated with Harvard. At the end of the seminar, Hastings called on the audience for comment or discussion and none was forthcoming. He therefore smiled at the speaker and said, "This is a very important paper, because this is the first time that these facts have been demonstrated at Harvard." The implication clearly was that until a finding had been confirmed in a Harvard laboratory it was not credible.

To be in medical science and to reside in Boston was a very happy arrangement. The strength in all the medical sciences distributed throughout that city was impressive. To visit with Joe Aub at the Massachusetts General Hospital and to go on rounds with Bill Castle at the Boston City Hospital were all fringe benefits. These two hospitals, together with Beth Israel and the Peter Bent Brigham, were the four major teaching hospitals of Harvard Medical School at that time. The distinction of the several clinical faculties was unmatched in the United States. Their clinical and research interests covered the entire

spectrum of medical matters. Harvard Medical School was governed by a mild mannered and gentle scholar, Dean Burwell. About once every month the entire faculty met under the dean's chairmanship to consider problems of importance to the medical school. These meetings, however, were dominated by the presence of James Bryant Conant, then president of Harvard University, who made it a matter of principle rarely or never to miss these meetings. It was reported that he managed to attend the faculty meetings on each of the approximately 10 campuses that made up Harvard University. He sat beside the dean and disposed of problems briskly. If any faculty member made so bold as to raise a question from the floor, Conant invariably responded by stating that the problem was one of great interest and thereupon referred it to a committee, naming the questioner as the chairman of the committee. Over the period while I attended these meetings, I noted that approximately four times as many committees were named as ever reported back. I learned from his performance the valuable administrative device whereby embarrassing or trivial questions may be forever buried. I recall that a perennial question at faculty meetings at Harvard Medical School related to the selection of army officers who would be in charge of the Officer Candidate School on this campus. Should he be selected by the medical faculty? Should we accept the candidate proposed by the United States Army? The matter was, I think, referred to a committee, but the final solution was made by the president in conjunction with the dean.

The winter of 1947-48 was a particularly severe one. In December 1947 the snow started to fall and it continued to fall for a long time. We had two cars in our family, but unfortunately throughout the winter one of the cars was trapped behind tons of snow in the garage, and the other was similarly trapped out in the street. Our steep and sunken driveway was buried in the snow for many months. I well recall that early in the winter it was discovered that the funds which had been appropriated by the city of Boston for snow clearance were found mysteriously to have vanished. The mayor of Boston at that time was James Curley, a skillful Irish politician who was serving a prison sentence as a result of a fraudulent sale of curbing stones to the city of Boston by some inmate of his. As soon as the snow started to fall, Mayor Curley seized time on the radio and in his impeccable Irish brogue addressed his faithful constituents approximately as follows: "The Lord has seen fit to deposit snow on the streets of the city of Boston. What the Lord hath given, let the Lord take

away. The city of Boston will do nothing whatsoever to interfere with the ways of the Lord." Thus did Mayor Curley ensure his continued reelection.

I enjoyed good relations with Baird Hastings who apparently was anxious to have me stay in the Department of Physiological Chemistry. To this end he had discussions with a friend and schoolmate of his who was then president of Arthur D. Little, Inc., and it was arranged that this expanding consulting firm would be willing to endow a professorship in physiological chemistry at Harvard Medical School with the proviso that the incumbent serve one day each month as a consultant to Arthur D. Little, Inc. It was Hastings' proposal that I should be the incumbent, and this arrangement was agreeable to me. I felt that to work with the industrial house could only broaden my experience. However, when the proposal was brought to the attention of President Conant, he immediately vetoed it on the curious ground that Harvard would then be beholden to an industrial concern. *O tempora, O mores!*

While I thoroughly enjoyed my teaching opportunities with the gifted members of the Harvard senior medical class, I was continuously frustrated in the laboratory by my inability to secure needed isotope analyses due to operating failure of the mass spectrometer. I was therefore receptive to a proposal presented to me by my former professor of medicine, Walter Palmer, who had by this time retired from P & S and had become director of the Public Health Research Institute of the City of New York. This unique institution, which will be described in more detail in the next chapter, was located at the eastern end of 15th Street in Manhattan and was composed of three laboratories. One of these, the laboratory of nutrition and physiology, was in a state of total disarray as a result of the development of a feud that was judged to be unresolvable. Palmer was brought down from P & S to make the peace and he determined that a new chief of this laboratory was required. The existing members of the laboratory left, thus creating a substantial vacancy. I was invited to assume this interesting position, and at the same time my salary would be doubled. The temptation proved too great.

In retrospect, I have on occasion wondered whether I would not have fared better had I remained at Harvard. Over the immediately ensuing years I received a number of attractive position offers at the level of department chairman at various medical schools, which I declined, not wanting to move again so soon. Had I remained in Boston at this time, I should probably have remained in academic institutions for my professional life. The combination of

Walter Palmer's genial invitation, the opportunity to create an entire laboratory, my exasperation with certain phases of the Harvard biophysics laboratory, and the uncertainties of ever achieving tenure at Harvard all favored the move. So once again Marney and I, together with our two small daughters, headed for New York and looked at homes in Riverdale. We brought with us a number of Harvard associates. These included Yale Topper, a gifted organic chemist who had been working in Baird Hastings' laboratory, Sidney Soloway, a Ph.D. candidate under Art Solomon, and the master technician, Frank Rennie. To this nucleus others were added, as will be discussed in the next chapter.

Chapter VIII

THE FOOT OF EAST 15TH STREET

Many, many years ago, the Port of New York was confronted with the problem of what to do with the crew and passengers on ships arriving at New York contaminated with infectious disease, most prominently yellow fever. Such ships were said to be in quarantine and were required to display the yellow flag which presumably related to yellow fever. The word quarantine, of course, referred to the 40 days which by tradition was the period of isolation required of infected persons. Undoubtedly other diseases such as cholera, dysentery, and smallpox were subject to similar isolation procedures. We are told that the statutes of the City of New York made it illegal to bring persons off of such ships into the precincts of the city, and for this reason an isolation hospital, a pesthouse, was constructed on a wharf in the East River, technically outside of Manhattan and therefore lacking a numerical street address. The assigned address was simply The Foot of East 15th Street. The name of the institution was the Willard Tarker Hospital. This area has since been filled in and the hospital has been dismantled, but in our time it existed and was in fact a rather busy place. Here were sent victims of all those communicable diseases who were denied admission to other hospitals in the city. While a medical student on pediatrics in the 1930s, I was sent down to Willard Parker to see cases of diphtheria, scarlet fever, and the like, and to learn something of the elaborate isolation precautions that were required. On the grounds of Willard Parker Hospital was a laboratory building originally occupied by the Board of Health of the City of New York, and its address also was The Foot of East 15th Street.

In 1928, Wall Street was in the midst of a great bull market. Everyone had large margin accounts, and paper assets of investors were growing astronomically. Among these was a wealthy young man, Mr. David Heyman. The tension under which he lived was such that he developed signs and symptoms suggestive of a peptic ulcer. His physicians therefore urged him to get out of the market and spend several months away from home. After some deliberation he accepted this advice. Shortly thereafter came the market crash which would have cut deeply into Mr. Heyman's fortune. He reacted to this situation in an unusual

fashion. He felt that the preservation of his fortune was the result of excellent advice from his physicians, and he therefore determined to devote the rest of his life and energies to the benefit of medicine. He had himself appointed to the city's Board of Health and here he made friends with a distinguished virologist from the Rockefeller Institute, Dr. Thomas Rivers. It was their view that basic scientific research was the most urgent need of medical science and that this would be poorly supported within the bureaucracy of a city board of health. Therefore, with the support of the health commissioner, Dr. Parkes, they proposed a novel structure which came to be known as the Public Health Research Institute of the City of New York, Inc. (PSRI). This agency was to be supported by a long-term contract with the City of New York which would contribute initially \$100,000 a year to this end. The choice of science and scientists in this institute would be determined by a top quality scientific committee headed by Tom Rivers.

This plan was presented to the energetic and imaginative mayor of New York, Fiorello La Guardia. He apparently liked the idea but was unable to find the necessary funds. Sometime thereafter it was determined to demand that all marriage licenses issued in New York require that premarital Wasserman tests for syphilis be performed upon both parties. Dave Heyman came up with the notion that if the city undertook to perform these tests, it might charge for the service rendered to the engaged couples and from this source \$100,000 a year could easily be collected. This additional source of city income would be enough to defray the cost of the proposed institute. La Guardia accepted this argument, even though almost immediately he found ways of conducting the blood test without the necessity of charging for the service. Thus the Public Health Research Institute was founded and was housed in the laboratory building on The Foot of East 15th Street. Soon there were three laboratories in the institute-- one headed by Jules Freund, a distinguished innovator in immunology and still remembered as the discoverer of Freund's adjuvant, a mystical mixture which when added to an antigen enormously enhanced the antibody response; the second by George Hirst, a disciple of Rivers and one of the most imaginative virologists of his time; and a third by Otto Bessey, whose background was chiefly in the field of nutrition. Bessey added to his staff Oliver Lowry, an investigator who was to make his reputation in the development of exquisite micro-analytic procedures for various enzymes, particularly of the central nervous system. These three laboratories shared the funds placed at their disposal and

had no specific obligations other than to conduct the very best research of which they were capable. It was an almost ideal situation. There was freedom from any teaching burden, and since grant money was not readily available in those days anyhow, there was no need to write grant applications. An early director of the institute was Dr. Ralph Muckenfuss.

Things proceeded smoothly and productively. The city's contribution was renegotiated and by 1948 had reached \$400,000 annually, with a contract to run for 10 years, a most unusual procedure in city contracting. Dr. Muckenfuss joined the armed forces and went off to war. To fill the vacant office, the board selected Otto Bessey to become acting director, a position which he apparently very much enjoyed. And so it came to pass that when Dr. Muckenfuss returned from the wars as a hero he found his office occupied, and at once a serious feud developed. Apparently Drs. Bessey and Muckenfuss had differences of opinion which could not be reconciled. Clearly, important decisions had to be made. A member of the scientific advisory board at this time was Michael Heidelberger, a biochemist and immunochemist and a member of the Department of Medicine at P & S. It was apparently at his suggestion that Dr. Walter Palmer, in the process of retiring from the chairmanship of the Department of Medicine, was selected to become director of PHRI, thus replacing Dr. Muckenfuss. It was Palmer's decision that things would operate better if Dr. Bessey also left. Bessey at once found a position at the University of Illinois Medical School in Chicago, and Ollie Lowry moved to the Department of Pharmacology at Washington University in St. Louis. Within a short time the laboratory of nutrition and physiology was essentially cleaned out. It was at this point that Walter Palmer invited me to come down from Harvard to look at this position. After studying the situation, I became convinced that here was a remarkable opportunity. Dr. Palmer had dreams of a new building for the Institute which he hoped would be close to and affiliated with P & S. He was able to place at my disposal a sum of money for installation expenses and to provide salary for a substantial number of supporting staff. In addition to Marney and myself, positions were provided for Yale Topper, Jean Benedict, Sidney Soloway, and Frank Rennie--all from Harvard. A number of additional positions were subsequently added including those of Frank Eisenberg, Irwin Leder, and Ben Bloom, plus technical and secretarial support. Furthermore, it was possible to accommodate an extraordinary group of postdoctoral fellows who became available because of a peculiar circumstance. Dr. James A. Shannon, who had moved to the

NIH in the mid-1940s as scientific director of the National Heart Institute, was planning for the completion of a vast new laboratory building at Bethesda to be called the Clinical Center. In anticipation of the completion of this building he had recruited a number of very able young physicians who were dedicated to the performance of research. Then, as so frequently happens, the building came in late. Jim Shannon had made commitments both to Leonard Laster and to James Wyngaarden and he found that he could accommodate neither. He therefore called me in the hope that they might spend time in my New York laboratory. I was delighted with the arrangement and both of these young men became collaborators and firm friends. Among the postdoctorals of that era were Lloyd H. (Holly) Smith, later to become chairman of medicine at the University of California, San Francisco, and Marcel Roche of Caracas, Venezuela, who subsequently became director of the major research institution of his home country. All four of these men had their clinical training in the Harvard-affiliated hospitals and they were superb colleagues in the laboratory.

Marney and I, accompanied by our two growing daughters, Gail and Nancy, took up quarters in a splendid fieldstone fortress on Waldo Avenue in the Fieldston section of Riverdale. This was our most sumptuous home, having been previously owned by one of the Crane (plumbing fixture) families who had equipped it with seven bathrooms, each one furnished in a different color of ceramics. It did involve us in a painful commuting exercise since we had to drive to The Foot of East 15th Street and back every day. Riverdale was, and probably still is, one of the most attractive enclaves of private dwellings in greater New York. We found wonderful neighbors and good schooling for our children in the private schools. On one side of us lived the Levey family. Stan was a labor reporter for the New York Times and Franky was a working biologist at New York University. They had two sons appropriately aged to play with our two daughters and these became firm friends. On our other side lived the Sam Rubins. Sam was the founding owner of a perfume manufacturing company, Faberge. He was also a music lover and had an interest in charitable affairs. He personally supported journal libraries in the recreation rooms of the resident staffs of the several city hospitals and took some interest in what Marney and I were doing at PHRI. I well recall the questioning to which I would be subjected when we met-- trimming our mutual hedge, mowing our lawns, or shoveling snow from our driveways. He would begin by asking, "Now tell me again, what exactly is it that you do down there?" and I would explain to him how I spent my time synthesizing

biological compounds with isotopic labels, administering these materials to suitable experimental animals, and isolating from the tissues and excreta of these animals suspected products. These I then analyzed for isotope content and by such experiments was able to reconstruct metabolic pathways. To this he would nod intelligently and then ask the question, "And they pay you for doing that?" Mrs. Rubin, having reared her family, had now returned to academia and was securing a Ph.D. in anthropology with Margaret Mead. The Rubins had musicals from time to time in a large chapel-like room in their house to which we were invited.

Considerable excitement ran through Fieldston when it was learned that Duke Ellington was about to purchase a home there. I am happy to report that this little community had no problem whatsoever in accepting this remarkably creative and cultured black man. I have, of course, no way of knowing what reception might have been accorded to a less distinguished member of his race.

While in Boston I had expanded my interest in carpentry to the extent of constructing a very small sailboat, the "Raggedy." She was a double-knuckle pram with oak frames, plywood skin, and mahogany transoms. Her mast was of Sitka spruce. Her sail was cut and trimmed from a war surplus nylon parachute and her pennant was designed and sewn by Marney at the suggestion of the children. It exhibited an image of Raggedy Andy complete with large buttons for eyes. We thoroughly enjoyed this little boat for a number of years. I regret that it now hangs in disrepair from the roof of our Woods Hole garage and will probably never be rehabilitated.

After this experience, as may be imagined, I was unwilling to live without a shop, and in our home in Riverdale I found a large room in the basement for this purpose. I gradually acquired elementary power tools, a table saw and a lathe which I taught myself to use. The lathe I found a particularly satisfying instrument for one who would love to have been a sculptor but has no talent whatsoever in that direction. It generates an impressive abundance of wood shavings in a remarkably short time, and I recommend it as therapy for anyone who is excessively keyed up over intellectual matters.

It was during the later years at Waldo Avenue that I participated in the composition of the first edition of our textbook, Principles of Biochemistry, by Abraham White, Philip Handler, Emil Smith, and Dewitt Stetten, Jr. This was an engrossing and very time consuming job. Virtually every evening and every weekend, when I was not otherwise engaged, were devoted to preliminary study

and ultimate composition of this textbook. The four authors became very firm friends despite a number of strained circumstances in the course of production. Our principle was first to divide the material into four approximately equal pieces and assign each part to one or another of us. Each of us would then undertake to prepare the primary manuscript of his section which would then be circulated through the other three. Each author was entirely free to make corrections, to suggest changes, and to try to improve the writing of his colleagues. By the time my manuscript would return to me it might be almost unrecognizable. It was our feeling that the readers of this textbook would be quite unable to identify the chapters which each of us had initially composed. The exercise provided for me and I believe for my coauthors the very best possible opportunity to review the field of biochemistry in its most general sense, and to familiarize each one of us with those parts of biochemistry outside of our own particular areas of expertise. My major assignments were the chapters on the chemistry of lipids and of carbohydrates as well as the metabolism of these classes of substances.

In the course of production of this book, there were many memorable episodes. Perhaps the most dramatic occurred one evening when Abe White, who was the general editor, called me from his Manhattan residence with tears in his voice to announce that the whole project must now terminate. I inquired as to what had happened. It appeared that Abe had taken it upon himself to alter certain passages in a chapter that had originally been written by Phil Handler, neglecting to discuss the matter with Phil beforehand. When galley proofs were distributed for reading, Phil for the first time discovered that his priceless pearls of wisdom had been tampered with and in a fit of temper tore the galleys into small shreds, stuffed them in an envelope, and addressed the envelope to Abe White. Abe and I were both New Yorkers, while Phil resided in Durham, North Carolina, and Emil was at that time in Salt Lake City, Utah. Abe was in deep distress. He and Edna immediately came out to our house and discussed the problem with me. I knew Phil very well and assumed that sooner or later he would calm down. This he did within a day or two, and a few telephone calls restored harmony among the members of our quartet.

The last step before going to press was an editorial review by a style editor working for the publishing house of McGraw-Hill. The young woman selected was, indeed, young--a recent graduate, I believe, of Vassar College. Her knowledge of biochemistry was nil but she was presumably an authority on

matters of punctuation, spelling, and literary style. The one principle to which she adhered most rigorously was that hyphens were no longer in fashion. She therefore systematically went through our painfully prepared manuscript and deleted every hyphen, sometimes eliding the two words and sometimes letting the empty space between them remain. My own taste in hyphens is poorly developed. I can take them or leave them. I did, however, balk when I suddenly encountered the word "crossstriations." I knew for a fact that triple S's were extremely rare in the English language. Therefore, one day in her office in the McGraw-Hill Building on 42nd Street in Manhattan I took her to task. She stuck to her guns and said to place a hyphen in crossstriations was contrary to the best current practices. I glanced around the room and saw that the bookshelves were filled with volumes recently published by the McGraw-Hill Book Company and I therefore offered her the following bargain: "I shall be happy to admit crossstriations without a hyphen provided you delete the hyphen from McGraw-Hill." She looked around the room in shocked horror, and instantly the hyphen reappeared in "cross-striations." It was the only argument with the McGraw-Hill Company that I ever won.

The book was published in 1954. It captured the field and was accepted by most medical schools in the United States, Canada, and England. In subsequent editions it was translated into other languages and it continues even now to be a much-used text. I dropped out of authorship after the second edition. At that point I had assumed heavy administrative duties and simply could not find the time and energy to continue with the book.

Meanwhile my job at PHRI was an essentially unalloyed success. I had a fine group of collaborators. I got along splendidly with the chiefs of the other two laboratories, George Hirst and Jules Freund, and was very happy under the presidency of Walter Palmer, an intelligent, witty, and genial physician and scientist. True, the building which housed our laboratory was old and crumbling but I have long known that the happiness in a laboratory and the quality of research coming out of a laboratory are not closely related to the splendor of the building. I became increasingly involved in a study of the nature of the metabolic defect in gout and made some contributions to an analogous study of muscular dystrophy. I found excellent clinical collaboration in the person of Alexander B. Gutman, a great physician whom I had known slightly at Columbia and who had moved to Welfare Island and subsequently to Mount Sinai Hospital. He and his associate, a very loyal Chinese physician named Dr. T. F. Yu,

produced all the patients we needed and meticulously collected all the samples that had to be secured. Jean Benedict, meanwhile, synthesized the isotopically labeled precursors that we administered, while Sidney Soloway and Frank Rennie had no difficulty in operating a mass spectrometer that we had purchased from a very small Brooklyn concern called Process and Instruments. This machine was built to our specifications and operated remarkably well. As at Columbia, the original instrument employed a D'Arsonval galvanometer for its final readout. I remember the pleasure we took when we replaced this extremely vibration-sensitive instrument with a far more stable vibrating reed electrometer that had recently been introduced by the Consolidated Engineering Company of Pasadena, California. It was also in this era that we first started to use in increasing amount radioactive carbon-14 which was much more readily available than the stable carbon-13. By this time, Geiger-Muller tubes could be purchased so we were spared the necessity of making our own. However, there was not on the market any device that was able to scan a paper strip chromatogram for radioactivity. Therefore, Sidney Soloway, Frank Rennie, and I put our heads and hands together and constructed such a piece of equipment. Our instrument was by modern standards clumsy and relatively insensitive, but it did function and it merited a separate writeup in the chemical literature. It fell to my lot to produce those parts of the mechanism which had to be built on a wood lathe.

I continued in these years to take a hand in many laboratory exercises. Thus Marney and I together found need to prepare some uniformly labeled glucose, not then available commercially. This we did by an approved procedure of placing beansprouts under intense electric light in a vacuum desiccator, the gas phase of which was then replaced by carbon dioxide containing ^{14}C . Under these circumstances the green leaves assimilate $^{14}\text{C}_2$ from the atmosphere and promptly incorporate ^{14}C into the starch which they synthesize. For its time, this was an exciting synthesis involving what was for us a substantial amount of radioactive isotope. Happily, we had no spills and no accidents, recovered the unreacted carbon dioxide, and isolated the starch and prepared glucose from it in satisfactory fashion. Another synthesis that I carried through by myself was in conjunction with a study in collaboration with Ben Bloom. We needed for this study some doubly labeled L- $(^{15}\text{N}^{14}\text{C})$ -arginine. This required the initial preparation of some cyanogen bromide which, in addition to being highly poisonous) was in this case highly enriched with isotope. The all-glass gas train

had to be homemade and could not be allowed to break or leak during the reaction. It was all rather exciting to make the apparatus as well as to run the reaction.

It is an article of dogma that man and the higher primates lack the enzyme uricase which in other species of animal oxidatively disrupts the purine ring of uric acid. We had now a very sensitive means of testing this dogma. A large batch of ^{15}N -uric acid was prepared and a portion of this administered by vein to Jim Wyngaarden. He subsequently isolated urea and ammonia from his own urine and demonstrated, to our chagrin and surprise, an appreciable amount of ^{15}N in these products, indicating that uric acid was indeed unstable in his body. The possibility existed, however, that what we had observed was the result of the action of bacterial uricase which we knew to exist in the bacteria of the intestinal tract. We therefore subjected poor Jim to massive doses of intestinal antibiotics, and after we had effected fairly complete sterilization of his feces we repeated the experiment. To our delight, there was now virtually no evidence of uric acid breakdown. We published these results only to learn subsequently that they disagreed with some results of others. The discrepancy has to my knowledge never been resolved.

It was during these years that Jarvis (Jay) Seegmiller came from the National Institutes of Health to join our group. He had been trained in medicine at the University of Chicago and had worked for some time in the laboratory of Bernard Horecker in the National Institute of Arthritis and Metabolic Diseases. He had an interest in learning about both the disease gout and the still novel use of isotopes in biomedical research. Together we gave much consideration to the nature of the metabolic defect in gout, a problem which had first concerned me during my days at Harvard. Using patients supplied by Drs. Gutman and Yu, we studied the rates of uric acid synthesis in normal and in gouty persons and concluded that, at least in the sample of patients which came under our scrutiny, the hyperuricemia of gout was attributable to excessively rapid synthesis rather than to impaired elimination. We continued to find enormous enhancement of the miscible pool of uric acid in gouty individuals. Over succeeding years at NIH and later at the University of California, San Diego, Jay Seegmiller has persevered in his studies of uric acid metabolism in health and disease. He refined our original observation on hyperuricemia and made a very important series of observations on young patients suffering from a bizarre disease--Lesch-Nyhan disease--identifying clearly the specific

enzyme defect which underlies this curious sex-linked genetic disorder. He furthermore was able to employ the demonstrated enzyme defect in this disease to prove in the mothers of such patients the actual occurrence of what has been referred to as the Lyon hypothesis--namely, that only one of the two X chromosomes in the female somatic cell is actually expressed and that the selection appears to be random. Although now separated by the entire continent, Jay and I continue to be close friends and visit with each other on all possible occasions.

The Public Health Research Institute of the City of New York, Inc., was at that time a remarkable institution. The entire staff comprised approximately 40 people and we all lunched together around several long tables. Walter Palmer routinely joined us, invariably climaxing his lunch with a large apple which he would carefully and ostentatiously peel with a large gold-handled pocket knife. Conversation about the board was very lively and wide ranging. This was the only institution with which I have ever been associated that had no deadwood whatsoever. Everyone eagerly pulled his or her weight and the research output was remarkably high both in quality and in quantity. These were certainly the most productive years of my scientific life and a good number of papers appeared between 1948 and 1954. Marney also enjoyed considerable scientific productivity and we collaborated on some projects. One of these was the composition of an article for Physiological Reviews on the subject of glycogen metabolism. This was a serious and scholarly effort and we both took considerable pride in the good reception that it was accorded.

It was during these years that we completed our family, adding first Mary in 1950 and finally George in 1953 to Gail and Nancy. Marney's deliveries were all performed at the Doctor's Hospital on the East River at about 81st Street, under the watchful care of Dr. Norman Pleshette, an old friend of mine from much earlier times. The deliveries were in no way remarkable and all four of our babies were entirely normal. It is true that Mary, soon after delivery, was noted to have a moderate fever which was subsequently studied at the Baby's Hospital and finally attributed to the excessively high temperature in the hospital nursery. At home we obviously had to have full-time sleep-in help at all times, and this we were always able to secure. Mrs. Sweet came down with us from Boston and stayed with us for several years. She was then replaced by Mildred Webster, who was an elegant cook with a somewhat obscure past and a definite taste for the ponies. In fact, she subscribed to the "Daily Racing

Form" and telephoned her bookie every day. Her great fondness for our latest baby biased her betting in favor of a filly named "Baby Mary," who I believe won very few races. When Mildred departed, she left an unpaid bill for \$40 with the newsman who had been delivering her "Daily Racing Form." Ursula Vogt, who came next, was a product of Nazi Germany. She was a high school teacher's daughter raised in the Hitler era in a small German town which had been incorporated into East Germany after the war. We felt impelled to complete her education and help her perfect her English. Since she was a very bright young woman, very ambitious and industrious, she reacted favorably to the academic environment of our home. Domestic service proved insufficient for her aspirations and she finally departed to take a secretarial job in a business organization.

Dogs were an important part of our lives and we always had either one or two. Our first dog, Marcus, was our only failure. On the morning of Sunday, December 7, 1941, I was lying in bed contemplating the novel problem of what to get my wife for a Christmas present. She had repeatedly told me of the adored Gordon setter, Jack, with whom she had grown up in Westfield, New Jersey. I therefore scanned the dog page of the Sunday Times but found no advertisement for Gordon setters. I did, however, find a New Jersey breeder offering registered springer spaniel puppies. We drove to the designated kennel and tentatively selected a liver-and-white male puppy. The dogs were in outdoor runs and I asked to see how the dog performed indoors. We entered the breeder's home and almost immediately a voice on the radio told us that the Japanese were bombing Pearl Harbor. Somehow this news clinched the sale and so Audley Farms Marcus, seated in a shoe box, came home to our apartment with us. Our concerns with this puppy were sufficiently large that we never did learn much of the early days of our entry into World War II. Marcus was descended from a long line of hunting dogs but in New York City varieties of game were limited. On Riverside Drive were many pigeons and Marcus would seek these out and "point," head down, tail aquiver, and right front paw raised. He would have been willing to hold his point indefinitely but the pigeons were unfamiliar with the rules of the game and walked away unconcerned. In the apartment, which like all New York apartments was cockroach infested, Marcus would stalk these creatures, sniffing at them with his large muzzle. Occasionally he would get so close and inhale so vigorously as to capture a roach in his nose. Whereas he was devoted to Marney and me, he was also jealous and difficult to manage.

Shortly before Gail's birth we thought it well to get rid of him. After several unsuccessful attempts to give him away, we returned him to his breeder.

While we were living in Riverdale, we got our first beagle through the good offices of Dr. Beatrice Siegel of P & S. Dr. Siegel had an ongoing study of the toxemias of pregnancy for which purpose she needed many pregnant female dogs. The males of the litters were of limited interest to her, and these she consequently sold to her friends at the then standard laboratory dog charge of \$8. I well recall the day when Marney and I took Gail and Nancy to Dr. Siegel's laboratory to inspect the latest litter. The kids selected what was obviously the cutest of the pups and we brought him home and promptly named him Sparkey after a dog which I had owned when I was a small boy. Sparkey was with us for about fourteen years. He was an affectionate if stupid dog, but he clearly had a charmed life. While still a puppy with oversized ears and a long wagging tail, he managed to get himself run over by a truck. He immediately took off for the underbrush and disappeared. For many hours we searched for him and finally he came walking back with obvious tire tracks still recognizable on his ear. Apparently the truck had only run over his ear and other than causing pain and a small laceration did no serious damage. He recovered from this and a number of other encounters with automobiles during his long life. He was affectionate, omnivorous (he rather favored aluminum foil), and quite unteachable. Sparkey moved with us to Chevy Chase in 1954. Some years later, after one of his solo excursions, he returned to our house with a definite limp. He had done this previously and we always assumed that the injuries were the result of encounters with automobiles. This time the limp persisted for several weeks and we finally took him to the Friendship Veterinary Hospital. Here he was diagnosed as having torn the cruciate ligament in his right knee. Since Washington had no veterinary orthopedist, the elaborate orthopedic surgery that was required to cure Sparkey was performed at the University of Pennsylvania's College of Veterinary Medicine, and he was returned to us in good health and lived for many years thereafter. He moved on with us to New Brunswick, New Jersey, where he lorded it over a series of Labrador retrievers before he finally died of a generalized carcinomatosis.

In 1965, while I was convalescing from a myocardial infarct, Marney, Mary, and George visited a breeder of Labrador retrievers and acquired our most satisfactory of dogs, Nicky. He was a black Lab from a distinguished line of prize-winning dogs--strong, affectionate, and very intelligent. He won his way

into all our hearts and was deeply mourned when he finally died years later of cancer after our return to Bethesda. Marney and I continue to miss Nick, a dog who clearly did not recognize that he was other than human. He regarded himself as one of our family and succeeded in convincing us that this was indeed so. Several years before Nick's death, Marney discovered a nearly frozen stray in a snowbank in our yard in New Jersey whom she promptly adopted with an assist from our then housekeeper, Wilma. The dog, whom we called Daisy, is probably a thoroughbred Tibetan terrier and has given us considerable pleasure. She is, however, no replacement for black Nick.

During my stay at PHRI I received several flattering offers from the outside. I was approached by the search committee for the chairmanship of biochemistry at Duke University shortly after our move to New York. This I had no difficulty in turning aside, partly out of a sense of loyalty to Walter Palmer and partly because my friend Philip Handler wanted the job very badly. Phil, indeed, did become chairman of the Duke department and served there with distinction for many years. I also was visited by the dean of the new medical faculty that was being assembled at Seattle, Washington. This was a challenging opportunity, but again I withdrew my name feeling that I had a better opportunity where I was. Several years later I was approached by James Shannon to consider the scientific directorship of the National Heart Institute (NHI), which would have placed me in charge of all the intramural activities of that institute. I went to Bethesda to explore the possibility and met with many old friends, including Chris Anfinsen, Bob Berliner, and Earl Stadtman. I was then presented to the Director of the NHI, Dr. James Watt, and discussed with him the role of the scientific director. He indicated that it would be my function to try to keep the research activities in line with the mission of the NHI as he saw it, which was ultimately to eliminate or control diseases of the heart. I inquired whether this meant that I was to persuade Earl Stadtman to discontinue his researches on anaerobic microorganisms and devote his attention to the enzyme structure of myocardium. Dr. Watt's face lit up in response to this suggestion and he indicated that this would indeed be a fine thing to do. Because I found this stress on categorical research distasteful, I immediately determined to decline the job and to remain in New York.

Undoubtedly I accomplished more scientific research during my tenure at the PHRI than at any other time. The group of coworkers that I had assembled proved to be exceptionally congenial and the administration of the laboratory

was amazingly simple. With Walter Palmer as my boss, I enjoyed very happy relations. Each year I would present an annual report of scientific accomplishments of the laboratory and, based upon this, I would submit my budget request. The fiscal situation of PHRI was such that with very few exceptions I received everything that I requested. Then once every year I attended a luncheon with the board of scientific advisors. During the early years I applied for no outside money because none was required. In the latter years of my stay I did apply to the NIH for a small sum earmarked for the purchase of isotopic precursors. None of the salaries of any of my colleagues was supported by outside funds, and during my stay the contract with the city was renegotiated to run for a period of 17 years. I started a seminar series in which the representatives of the other two laboratories participated, and we invited many distinguished scientists from the New York area to talk to us. I particularly recall seminars by Otto Loewi on chemical transmission of neural impulses, and by Homer Smith who was invited to talk on kidney function but actually spoke mostly on his favorite subject, atheism.

During these years in New York I did little formal teaching, giving only occasional lectures at Columbia or at the New York University College of Medicine. I did, from time to time, attend the Saturday morning combined clinics at P & S, which were always lively discussions of topics of current medical interest. Also during these years I served on several editorial boards, among others the Journal of Biological Chemistry and Metabolism. During the last years in New York I was appointed to the biochemistry and metabolism study section of the NIH, which brought me to Bethesda three times each year to review grant applications. Prominent on that study section was Dr. John Peters, a professor of medicine at Yale University, who at that time was in the throes of an argument with Senator Joseph McCarthy of Wisconsin, an argument which ultimately resulted in his being discharged from the study section. What appeared to be a completely trumped-up charge that he had Communist affiliations offended several of us very deeply. I resigned from the study section in protest at that time.

This service on an NIH study section was not my first exposure to the peer review system. Several years earlier I had been invited to attend the first meeting of the "Committee on Growth" of the National Research Council. This ad hoc committee was assembled to distribute research dollars that were left over from World War II appropriations among scientists who were working on one or

another aspect of cancer. We all met in the ballroom of a Washington hotel and were seated around tables in groups of about six or eight. I remember that at my table the chairman was Fritz Lipmann. Another member of the panel was Philip Cohen of Wisconsin. Summaries of research proposals were presented to us and were given a merit ranking by the group. The operation of an NIH study section was far more formal and I believe far more thorough. Each member of the study section received some weeks before the meeting a large stack of applications, usually no fewer than 80 and sometimes as many as 120. These he was supposed to read, paying particular attention to a designated few on which he was either the first- or the second-named reviewer. The meeting was convened generally in Bethesda, either in a room at the NIH or in one of the motels in the neighborhood, where under the guidance of the chairman and the executive secretary each application in turn was discussed in considerable detail. The initial presentation was always made by the member who had been designated as first reviewer. After sometimes heated discussion, a poll was taken in which each member around the table independently rated the application on a scale of from 1 to 5. The "priority score" was based upon the average of these individual scores and served as the basis for the funding/nonfunding decision by the institute. The study sections have always taken their work extremely seriously and function honestly and well. Each study section member is pledged to take no advantage of the information made available to him in the application and I believe this enjoinder is almost universally honored. Not surprisingly, all applicants who fail to receive funding feel that they have been treated unfairly and many of them protest to one or another officer at NIH. I believe in general these protests are unjustified.

The final years of my stay at the PHRI were marred by Dr. Palmer's death. He was succeeded by Dr. L. Wittington Gorham, formerly professor of medicine at Albany Medical College. Under his directorship, morale deteriorated perceptibly in the institute and this contributed to my willingness to listen to new overtures from the NIH. By this time Shannon was the Deputy Director of NIH, and Henry Sebrell, a nutritionist, whom I had known through common scientific interests, was the Director. I was approached by representatives of the National Institute of Arthritis and Metabolic Diseases (NIAMD) in the persons of Floyd Daft, whom I had known through service on the Macy Foundation's Committee on Liver Disease, and Joe Bunim, who had been my resident while I was an intern at Bellevue and who now was clinical director of NIAMD. The prospect

of moving to this institute was brightened by the persuasions of three junior colleagues in the laboratory: Lenny Laster, Jay Seegmiller, and Jim Wyngaarden, all of whom had titles in NIAMD. The Clinical Center was now essentially completed and considerable laboratory space had become available. It was made possible for me to move my entire group of associates from PHRI down to Bethesda and this increased the attractiveness of the offer. We created the section on intermediary metabolism of the laboratory of biochemistry and metabolism, NIAMD. In addition to serving as chief of the section, I became scientific director of the institute. The year was 1954 and the NIH was clearly in the ascendant. There were great things to be done in Bethesda. Therefore, and with certain nostalgic twinges, we tore up our New York roots and moved to Bethesda. The move was preceded by several months of commutation on my part and the usual troublesome headache of house hunting in an unfamiliar environment. We finally sold our Riverdale home and bought a house in Chevy Chase, Maryland.

Chapter IX

ARTHRITIS AND METABOLIC DISEASES

The National Institutes of Health was in 1954 in a phase of rapid growth. The Clinical Center, by far the largest of the many research buildings on its campus, had just been completed. It contained, in addition to many laboratories, a unique facility for the conduct of research on human subjects. It was in fact a research hospital with more than 500 beds, by far the largest such installation in the world. Annual appropriations to the several institutes were increasing every year. Scientists and supporting staff were being added. Each institute had a large grants program, and various types of training programs were being initiated. Bethesda had become the hub of the biomedical research universe.

At the time of our move, the wing of the 9th floor of the Clinical Center that had been assigned to us was still incomplete. This wing of approximately 5,000 square feet of net space was still without partitions, without plumbing, and without wiring, and we quickly drew up plans designed to make this space most useful to our needs. It was divided into a variety of one- and two-module laboratories, cold room, chemical stockroom, instrument room, darkroom, offices, and library-conference room. The basic design of this very modern laboratory building was such that the partitions and the laboratory equipment were all interchangeable and designed for rapid mounting and demounting. Nonetheless, it took the better part of a year for the workmen to finish off our designated space. In the meantime, we occupied an adjacent wing which had been designed and completed for occupancy by the laboratory of a colleague, Dr. Bernard Horecker, who was distinctly irritated by this preemption of his space. So Bernie and his colleagues had to remain in Building 3 for several additional months before we could move into our new laboratories and he into his. Although relations between the two adjacent sections may have been stressed initially, I am happy to say that eventually all was forgiven.

Departure from PHRI was not particularly painful, since I was taking my whole gang with me. Departure from our beautiful home in Riverdale, on the other hand, caused considerable sadness. We had no difficulty whatsoever in selling our Riverdale home to a physician and fellow diabetologist, who visited

it one Sunday in our absence, accepted our price without question, and purchased the home over the telephone that evening. It subsequently developed that he had not even taken the time to count our magnificent array of bathrooms. The purchase of a new home in Maryland was somewhat more difficult. We finally selected a new house at 7504 Maple Avenue, Chevy Chase, next door to the house of Joe Bunim and his family. Whereas our new house was far more compact than the one we left behind, the location was extremely practical, it being within walking distance of the grade school, the intermediate school, and the high school. Also within walking distance were music teachers, dance teachers, a Girl Scout troop, and a variety of other activities useful to a growing family. The children and Sparkey, our beagle, adapted very well to the new environment and it was here that our children really grew up. Montgomery County at that time had an excellent public school system, a reflection of the relatively high academic background of its population. Up and down our street virtually every house had one family member with a doctoral degree and a number of houses had two. Since the activities of the Parent-Teacher Associations were taken very seriously, it is not surprising that the inhabitants of Chevy Chase demanded and secured high-quality schooling for their children.

The section on intermediary metabolism housed a group of scientists whom I brought with me from New York. These included Yale Topper, Frank Eisenberg, Frank Tietz, Irwin Leder, Ben Bloom, and, of course, Marney. Each of these has pursued his own research interests. Yale has been particularly interested in the hormonal control of the activation of the cells of the mammary gland and the phenomenon of lactation. When I determined that I should no longer serve as chief of the section, that title devolved upon him. Frank Eisenberg had developed an interest in the biochemistry of inositol and its derivatives and has continued over the years to pursue the enzymes and the reactions relevant to this curious compound. Marney's interests at the time were in problems of glycogen chemistry and metabolism and for a number of years we collaborated on some of these problems. Her researches since that time have taken her into the clusters of enzymes that are found in the microsomal fraction of liver homogenates. She has presented evidence that several activities, including glucose-6 phosphatase, inorganic pyrophosphatase, and a previously unsuspected pyrophosphate-glucose phosphotransferase, may all reside in one and the same protein. More recently, as a result of our visits to Woods Hole and her summer activities at the Marine Biological Laboratory, she has developed a fondness

for invertebrate forms and has been applying her techniques to a study of enzymes of the hepatopancreas of various invertebrates, including *Limulus polyphemus* (the horseshoe crab).

In addition, over the years we picked up a number of associates. Among the postdoctoral fellows who worked closely with me was John H. Bryant, a physician trained at Presbyterian Hospital in New York, a man of high missionary zeal who wanted to round out his education by an experience in a research environment. Jack and his wife, Nancy, met while both were working at the Grenfell Mission in Canada, a hospital devoted to the treatment of tuberculosis among the Eskimo population. He elected to work on a problem that was introduced into the literature by Lewis Thomas. Thomas had shown that an injection of crude papain, a proteolytic enzyme from pineapple, into the vein of a rabbit caused the rabbit's ears to droop. The pictures of these pathetic animals made them look like a cross between a rabbit and a spaniel dog. Several days after the injection the ears would be restored to their normal attitude. The question which we raised was one of the mechanism of this extraordinary event, and Jack was able to show that commercial papain, in addition to its major proteolytic component, contained also an enzyme capable of hydrolyzing the mucopolysaccharide of cartilage. In the course of this experiment we did produce some ridiculous-appearing rabbits, much to the delight of our visitors and our children. Jack and Nancy have had an interesting life subsequently. He has made a study of institutions of medical education in the Third World and served for a while as the dean of one of the medical schools in Bangkok. More recently he has been dean of the school of public health at Columbia University and then director of the office of international health in the Department of Health and Human Services.

Another gifted postdoctoral fellow who came to work with me was Marshall Nirenberg. It was during a meeting of the Federation of American Societies for Experimental Biology in Chicago in 1957 that Marshall first approached me. I well remember our sharing a cup of coffee and a doughnut in a grubby restaurant on the Chicago Loop while he explained to me the troubles that he had at the University of Michigan and the reasons for his wanting to come to Bethesda. It was rapidly and easily arranged to provide Marshall with a postdoctoral fellowship, and he shortly joined our group in Bethesda. Marshall, a tall, thin, and very intense young man, selected his own area of research which was to ascertain the chemical difference between tumor and non-tumor cells. He elected to

study so-called Ehrlich ascites tumor cells which are grown in the peritoneal cavity of the mouse. He soon discovered that these cells were virtually devoid of glycogen, the storage form of sugar in most animal cells, and was ready to draw sweeping conclusions that this was indeed the chemical basis of cancer. I was able to persuade him to look at other tumors, and it turned out that the absence of glycogen was far from universal. It is probable that the cells of the Ehrlich ascites type are actually very malnourished, being free swimming and having no blood supply of their own. This appeared to be the most plausible explanation of their failure to store glycogen. They were, in effect, starving cells.

One day an unannounced visitor came to my office. He revealed himself to be Marshall's father, a retired merchant of modest circumstance residing in Florida. He expressed to me some concern about Marshall's future and raised the very question that my father had raised with me many years earlier: "Can he really make a living out of biochemistry?" I believe that I reassured him. Marshall was a very persevering investigator. When a vacancy occurred in the laboratory of Gordon M. Tomkins at the opposite end of the long corridor, Marshall was selected for that position and again he chose his own problem. This was to unscramble the genetic code, the existence of which had been postulated since the time of the publication of the Watson-Crick hypothesis in 1953. It was reasonably certain that the sequence of nucleotides in DNA contained the information that ultimately appeared as a sequence of amino acids in the corresponding protein. That the code was a triplet code, three adjacent nucleotides being required to encode for one amino acid, was also strongly inferred from purely numerical considerations. But at that point in history, no one could write a triplet of nucleotides that was known to correspond to any particular amino acid. It remained, for Marshall and his colleague, Johann Heinrich Matthaei, to perform their remarkable experiment using conditions which they had discovered for the synthesis of polypeptides in the total absence of any living cell and employing Leon Heppel's synthetic polyuridylic acid in place of a natural RNA. Under these circumstances, they found abundant incorporation of phenylalanine and of no other amino acid into their growing polypeptide, strongly suggesting that UUU encoded for phenylalanine. This indeed soon proved to be true, and over the ensuing years the entire code of 64 triplets lay revealed by their onslaughts.

I recall that Marshall's first discovery was made shortly before an international congress of biochemistry in Moscow which he was anxious to attend. As scientific director of the institute, it was my responsibility to allow or to withhold the privilege of such travel. I used this authority to compel Marshall to put his discovery in written form and submit it for publication before I would allow him to leave the United States. This proved to be a useful precaution because immediately after Marshall's announcement of his results in Moscow a number of other laboratories went to work on the problem, and he might well have been scooped if he had not been able to demonstrate prior submission for publication. His work was, of course, rewarded some years later by the awarding of the Nobel Prize.

My section over the years played host to a number of foreign visiting scientists, among these Shlomo Hestrin of Israel, Yoh Imai of Japan, Ernst Simon of Israel, and Costas Vlasopolous of Greece. These visitors clearly added significantly to the richness of the experiences shared by my colleagues and me.

The laboratory facilities that were provided to me and my group were very well appointed. This time, instead of building a mass spectrometer, we purchased one from Consolidated Engineering Corporation which, once aligned, functioned excellently for many years. It was an instrument designed specifically to determine isotope ratios, and this it did simply and rapidly with high reproducibility. My own laboratory activities were curbed by the fact that I now had responsibility for the administration of some 12 laboratories and clinical branches with approximately 200 doctoral scientists and a total population in the neighborhood of 500 persons. Much of our business, including review of all promotion actions, was conducted at weekly luncheon meetings of the laboratory and branch chiefs. It was also my duty to represent the intramural program of NIAMD at the meetings of the scientific directors of the several institutes every first and third Wednesday morning in Building One. These meetings were chaired initially by James Shannon, then by Joseph Smadel, and finally by G. Burroughs Mider. Here was the opportunity to compare and contrast the operation of the intramural programs of the several institutes. Here it was that some form of equity was preserved between them. This group, the scientific directors of NIH, in my opinion was and continues to be the most stimulating and interesting group that meets on a regular basis on the NIH campus.

Of the three deputy directors for science* under whom I served, Shannon was clearly the most creative. He was well grounded in medical sciences, a distinguished renal physiologist, and a director of one of the aspects of the wartime antimalarial program on Welfare Island, New York. He served briefly as an officer of Squibb, the pharmaceutical house in New Jersey, and then moved to Bethesda to assume control of the intramural program of the National Heart Institute. To this institute he brought many of the distinguished scientists upon whom its reputation was based. He was soon promoted to the post of associate director, NIH, serving under Director Henry Sebrell. Shannon was, in my experience, one of the greats--inquisitive, decisive, and generally cool tempered. He had developed since our Bellevue days into a very astute politician and a skillful manager of people. He recognized and appreciated quality in science and was unwilling to compromise. I always found him to be generally reserved in his personal relations. Over our many years of contact I was never invited into his home, but in our professional relations there were never any serious problems. It was his habit conversationally to probe into scientific matters.

I recall one day, while we were standing side by side in the cafeteria line in Building One, his asking me what all this stuff about entropy was. I therefore described to him a pack of playing cards as it, was received directly from the manufacturer. The cards were all arranged in order, ace through king, suit by suit, and the package was sealed. Such a package was then poised on the edge of a table and by the slightest movement of a finger it was tipped into space and fell to the ground, thus performing a certain amount of kinetic work upon the environment. To restore the package to its original condition, one simply had to lean down and pick it up and place it back on the table, performing an amount of work against gravity essentially identical to the work which the pack had performed on the environment during its descent. I then continued: "Let us now perform another experiment. Let us take the cards out of the container, still neatly stacked in order, and poise them on the edge of the table, and once again push them off the edge. This time, in order to restore the original set of conditions, it will be necessary to pick up the individual cards and rearrange them in the original order before placing them on the

*The title of this position has been fluid. What was once the associate director, NIH, and subsequently director of laboratories and clinics, is now called deputy director for science.

desk. During their descent they will have become randomized. The entropy of the pack will have increased, which is the spontaneously occurring event. In order to restore the pack to its original condition, additional work will have to be done over and above the work due to gravity; the cards this time will have to be replaced in their original order. This latter is entropic work. It is the work related to the restoration of order or to the overcoming of randomness." I was rather proud of this analogy and this pride may have shown in my face. At all odds, Shannon listened attentively and then said, "I don't believe a word of it!"

Joe Smadel was a scientific director of another character. He was brought to NIH from Walter Reed Army Medical Center because of his skill in virology to help solve the problems generated by the introduction of the Salk poliomyelitis vaccine. Joe was undoubtedly highly competent in his area. I found him to be a difficult man to work with. He was incisive, sometimes obstinate, and frequently lapsed into abusive language. My relations with him were not particularly happy. Joe habitually referred to our scientific colleagues as "jokers," "dopes," and "sons of bitches." A continuing topic of discussion by the scientific directors was the assignment of appropriate titles to the scientists. Thus, at the Rockefeller Institute scientists were classified as associates, associate members, and members, corresponding roughly to academic titles of assistant professor, associate professor, and professor. In the course of a meeting of the scientific directors, Joe Smadel presiding, I moved that we should formalize the titles that were actually in use and label our scientists as "jokers," "dopes," and "sons of bitches." As far as I can recall, the motion was never seconded.

When he finally took ill he was replaced by a colleague, G. Burroughs Mider, known as "Bo," who had been scientific director of the National Cancer Institute. Whereas Bo and I had been competitively situated, when he assumed his new position he became remarkably supportive of my hopes. A point at issue was Building 2. This building had been the home of the National Institute of Dental Research. However, NIDR was now moving into its own new palace, Building 30, leaving Building 2 up for grabs. There were two competitors--the NIAMD and the National Institute of Neurological Diseases and Blindness. The organizational plan that I presented to Bo Mider in his new capacity of Deputy Director met with his favor and Building 2 was assigned to NIAMD.

I was able to put together a laboratory of molecular biology centered about

Gordon Tomkins. Among its members were Gary Felsenfeld, a physical chemist from the Mellon Institute of Pittsburgh with an interest in nucleoproteins; David Davies, a British import who was our X-ray diffraction crystallographer; Harvey Itano, a Linus Pauling-trained chemist and co-discoverer with Pauling of the chemical nature of the defect in hemoglobin which results in sickle cell disease. Also in this group were Bruce Ames, who subsequently achieved great distinction by developing a method for the screening of compounds for mutagenicity and its application to widely distributed products such as fire-retardants and hair dyes, and Elizabeth Maxwell, who was a very loyal supporter of Gordy's own laboratory efforts. This cluster became one of the hot spots of research on the NIH campus and I have always regarded its establishment as one of the more positive contributions that I made to NIAMD and to NIH.

This calls to mind both my happiest and my saddest associations with the National Institutes of Health. Gordon Tomkins and I first encountered each other during my short stay at Harvard in 1947-48. He was one of the many medical students who elected to take the course that I offered in clinical aspects of biochemistry. I was wholly unaware of his presence at that time, but Gordon generously assured me much later that it was this course that determined his career in the direction of research rather than of medical practice. Gordy's father was a physician and his mother a piano teacher, and thus his heritage combined medical and musical matters. After graduating from the University of California, he entered Harvard Medical School where he earned his M.D. and followed this with an internship at the Peter Bent Brigham Hospital. He then returned to California to earn a Ph.D. in physiology under the guidance of I. L. Chaikoff, who also was the preceptor of my colleague Ben Bloom. Gordy was then brought to the NIH where he served first in the National Heart Institute and then in the NIAMD, and it was here that we renewed our acquaintanceship. Gordy was married to a former University of California fellow student, Millicent. She was extremely gifted as a singer of concert quality and as a painter who was able to exhibit and to sell her paintings. Gordy also had his share of talents. He was a versatile musician of professional quality, favoring the clarinet which he played both in the classical and in the jazz modes. He was in great demand at jam sessions and was fully accepted by the migrating population of professional jazz musicians. In addition, he played both the piano and the harpsichord. He had studied philosophy while at college and continued to read widely and deeply in this and related areas. As a research bio-

chemist he was interested in everything. His own research activities related to the monomeric-polymeric states of certain enzymes, the nature of endocrine signals to cells, and the concept of diseases of receptor sites. But his great talent was in the realm of communication with fellow scientists. Never have I known another who could exceed him in his ability to stimulate the interest of colleagues in scientific problems. Gordon could listen with total attention while a junior colleague presented his experiments, and then in an effortless fashion could point out important aspects of what he had just heard that had never occurred to the presenter. Many discouraged investigators, after a brief visit with Gordy, would return to their own laboratories fired up with a new enthusiasm, a new interest, and a new point of view. Gordy seemed to have all the qualities that were needed to extract the highest level of scientific productivity from his friends and associates. He developed a professional following at Bethesda which I think has not been matched since, and which was essentially unrelated either to his own position or to such prestige as he commanded. His benign influence upon the science and the scientists at NIH far exceeded the fruits of his own personal investigations. All of those who had much contact with him were in his intellectual debt.

When I later moved to Rutgers University to establish a medical school, Gordy Tomkins was the man I wanted to head my department of biochemistry. Unfortunately he elected not to move there. He had great troubles with outside job offers. His extreme good nature inclined him to accept, and his subsequent reflections led him to decline. He thus accepted and subsequently declined impressive offers from both Harvard and Yale Medical Schools. Finally, when an offer came from the University of California at San Francisco, he was unable to decline. So, in 1969, the Tomkins family moved to San Francisco where Gordy helped establish the excellent reputation of UCSF's Department of Biochemistry and Biophysics.

For a number of years his friends were concerned about Gordy's neurological health. Once during a seminar at NIH he had an epileptiform seizure, which was studied in the Neurological Institute to no avail. Subsequently he developed extreme tinnitus (ringing in the ears) which was particularly disturbing to one of high musical sensibility. After much study it was determined that he suffered from an acoustic neuroma. In 1975 he was referred to Mount Sinai Hospital, New York City, which had good experience in the surgical removal of this tumor. Unfortunately, the postoperative course was complicated by an

undiagnosed hemorrhage which led to massive brain destruction. Gordy never awoke from the operative anesthesia, and after a period of seven or eight weeks in coma he finally died. The outcome was particularly tragic since he was at that time only 49 years of age, at the peak of his scientific productivity, and was exerting a particularly strong positive influence upon a large group of friends and followers. His passing was and continues to be deeply mourned. I was invited out to California to participate in his memorial service. Because Gordy was an essentially joyous man, this service, conducted in a museum in San Francisco, was not as gloomy as it might have been. His many friends recalled the happy as well as the sad hours. The service was a curious mixture of scientific recollection and of music, to which his two daughters, both gifted musicians, contributed, as did the remnants of his former jazz combo. Gordon Tomkins Memorial Concerts continue as an annual event in San Francisco, where Millicent still paints beautiful pictures.

With my newly assumed administrative duties, my own laboratory activities decreased markedly. I did, however, take on responsibility for one final Ph.D. candidate, Howard Katzen, who was serving at that time as Marney's technician. The problem upon which he worked had to do with the purported assembly of the insulin molecule which contains two polypeptide chains linked to each other by two disulfide bridges. At that time the existence of preproinsulin, a single long polypeptide which served as parent to both the a and the b chains of the final insulin molecule, was not even suspected. It was assumed in many quarters that each of the chains was separately synthesized and subsequently brought together and we sought the enzyme responsible for this assembly. Howie was an extremely industrious laboratory worker. When he first came into the section, he had still to complete his baccalaureate studies at Johns Hopkins. We subsequently enrolled him as a graduate student at George Washington University with an assignment to perform his dissertation research at NIH. After earning his Ph.D. he took various jobs in Boston, Baltimore, and Bethesda, and finally moved to the research group at Merck in Rahway, New Jersey, where he has pursued his own basic science interests that have had to do with the description of the several enzyme systems responsible for the initial phosphorylation of glucose. With Jean Benedict, who had moved with me from Harvard to PHRI to NIH, I initiated studies designed to determine the mechanism of the succinic dehydrogenase reaction. These, however, came to naught and Jean wisely came to the conclusion that she would have a more

interesting time in the extramural programs of NIH. She has served a number of institutes in various extramural capacities.

During my tenure as scientific director at NIAMD, I was a party to several innovations. Among my fellow conspirators in these activities were Robert Berliner, the then scientific director of the National Heart Institute; Robert Livingston, scientific director of the National Institute of Neurological Diseases and Blindness; Seymour Kety, scientific director of the National Institute of Mental Health; and John Eberhart, who succeeded Kety. We all were more or less uncomfortable with the peculiar lack of democracy in the structure of the National Institutes of Health. The organization of this and I believe of most other Federal institutions is strictly hierarchical. By this I mean that at each level of authority the incumbent has almost total control of those beneath him but very little control over himself. He is, in turn, controlled by those above him. The structure is rigidly pyramidal, with the flow of information almost entirely from the top of the pyramid downward. The workers in the mines, particularly the gifted, independent scientists whom we had assembled, had very little to say about policy decisions of the NIH. This was in striking contrast to what I have seen in universities, where the voice of the faculty is loud and clear and cannot be denied by the top administration. There was no "faculty" at NIH and we decided that the institution could be strengthened if there were. What we therefore established in each of the interested institutes, and ultimately across the board at NIH generally, was "the assembly of scientists." In achieving this goal we received little or no support from NIH Director Jim Shannon, who viewed us, I think, as a bunch of radicals who threatened his authority. We secured a moderate degree of enthusiasm for our proposal among the scientists and, ultimately, the several assemblies of scientists were created. Their performance, I must admit, has been disappointing to me. Instead of functioning as a faculty usually functions --namely, as a positive body that creates new ideas and generates new policies, the meetings of the assemblies of scientists have often degenerated into "gripe sessions" in which the major topics of the discussion are often of a fairly trivial nature. I recall no occasion on which an assembly of scientists has come forward with an important novel policy that it wished to promulgate, although during my absence in 1962-1970, such events might have taken place. Still, we did establish a channel through which the views of the scientists could be transmitted upwards through the institute directors and

ultimately to the Director, NIH. And such a channel, even if rarely used, is I believe important to the dignity of the individual scientist.

A second and, in general, a more successful venture was our attempt to improve the quality of life on the Bethesda campus. This ultimately led to the establishment of the Foundation for Advanced Education in the Sciences, Inc. (FAES), an organization that has grown in vigor and in financial stability over the many years of its life. The NIH, as I found it, was in effect a research factory. Its product was the published fruits of research occurring in its laboratories and clinics. Some of us felt strongly that in the American culture research and teaching were not readily separable, and the NIH had no overt teaching function. Over the years there had grown up a series of courses offered in the evenings by members of the NIH staff, chiefly for members of the NIH staff. It all started with a course in enzyme chemistry offered by Alan Mehler, NIAMD. At that time the NIH had no authorization to sponsor such classes so we originally operated under an authorization from the Department of Agriculture. With the establishment of the FAES, this organization assumed complete responsibility for the evening classes and secured authorization for this activity from the Board of Education of the State of Maryland. The evening classes grew in popularity and in number, and at present on any weekday evening you can see students swarming into the limited number of conference rooms on the NIH campus to attend lectures usually given by NIH staff. Many of the students are postdoctoral research workers at the NIH who are upgrading their knowledge of their own fields or extending it into others. The catalog has grown until at present approximately 63 courses are offered each semester and about 3,000 students enroll. The fees are modest, as are the stipends paid to the instructors. The evening classes may be taken for credit at a number of colleges, although no degree-granting authority has been given to the school. Its long-time dean is Louis Cohen, an organic chemist in the NIAMD, and the success of the evening classes is largely due to his efforts and to the support given to him by the executive secretary of FAES, Mrs. Lois Kochanski.

An additional teaching function that we negotiated results in the production of a limited number of Ph.D.s. This program is a collaboration between FAES and the Department of Biology of the Johns Hopkins University. The students are enrolled by Johns Hopkins and elect to do their dissertation research under the sponsorship of qualified NIH scientists in NIH laboratories. This has

given to NIH the blessings of a population of predoctoral students, albeit modest in dimensions.

As FAES looked around the campus, there were a number of other activities that were curiously lacking. For instance, here we had a highly literate community, several thousand persons holding doctoral degrees, and yet there was no bookstore. Eventually space was secured in the basement of the Clinical Center, and FAES established a bookstore which it continues to run with increasing prosperity. Initially the rules were so interpreted as to make it impossible for the NIH to purchase books at the FAES bookstore. However, a more recent construction of the rules has opened up this possibility and the bookstore is now a flourishing venture.

The functions of the NIH being rather sharply delineated, we had very little in the way of decorative arts and nothing in the way of music. Both of these deficiencies the FAES has endeavored to correct. Starting with a gift from Seymour Kety, a fund has been set apart for the purchase of pictures, mostly prints, which are now displayed in the several cafeterias of the NIH. Apparently no appropriated Federal funds had been set aside for this purpose. This activity has for years been the particular interest of an enzyme chemist and colleague, William Jakoby. Then we discovered in our group a very gifted musical impresario in the person of Giulio Cantoni. He undertook to establish a concert series which has become a very important part of activities on our campus. On seven or eight Sundays during the year at 4 o'clock in the afternoon, he presents in NIH's largest auditorium for our delectation a soloist or a chamber music group which he has selected, with the support of Mrs. Saffiotti, the wife of an epidemiologist in the National Cancer Institute. Giulio always writes the program notes, which are both charming and scholarly, and his taste in performing artists is impeccable. These concerts are routinely reviewed in the pages of The Washington Post where they always seem to receive a glowing appreciation. The charges for admission have been kept low and the program in most years needs additional support from the Foundation.

Finally, it has long been the wish of the members of the FAES to build its own clubhouse. To this end, many years ago the Foundation purchased Chris Anfinsen's land when he ill-advisedly temporarily left the NIH to assume a professorship at Harvard Medical School. However, the Foundation never seemed to be able to accumulate sufficient funds to undertake the construction of such a club facility. Finally, it came to pass that the commissioned officers'

organization, which owned a modified private dwelling immediately adjoining NIH property needed financial assistance. The Foundation learned that by assuming the mortgage on this property it would acquire title to the building. This it has done and now the Foundation does have a house which is used for a variety of meetings, social purposes, and other functions. It is referred to as the Social and Academic Center. It has no license to serve food, but has recently secured a license to run a bar which is open certain afternoons each week. The operation of anything resembling a typical university faculty club still appears quite remote, although in my opinion this would be very desirable.

The Foundation is in a position to perform certain useful services to NIH. For instance, it acts as an agent in receiving and disbursing private grants which may be available to our guest workers. In addition, FAES is the agent that manages health insurance programs for our visiting staff. FAES also runs a series of occasional lectures on the NIH campus, inviting distinguished scientists from American and European institutions to make presentations before NIH audiences. In this function we supplement the already existing series of NIH lectures that were initiated at about the time the Clinical Center opened.

NIH intramural programs contain a large number of extraordinarily fine men and women, many of whom have become my close friends. It is not possible to give sketches of many of these, but I shall select from among my memories certain candidates for special attention. Even before I moved from New York to Bethesda, I started recruitment activities. Upon review of the structure of NIAMD I was struck by the fact that whereas there was a basic science laboratory devoted to endocrinology, headed at that time by Evelyn Anderson, there was no clinical branch of endocrinology. It appeared to me that this was an essential but missing component of our structure, and I therefore cast about for likely candidates. It was at a meeting of the Federation of American Societies for Experimental Biology in Atlantic City that I was introduced by Yale Topper to an extraordinary woman, Rosalind Pitt-Rivers, an enthusiastic, perceptive, very British lady with greying hair and a cheerful outlook on the world. She had been closely associated with Sir Charles Harrington in researches on the active thyroid hormones, thyroxin and triiodothyronine. At the end of the meeting, since I had a car and was driving to New York, Rosalind shared the ride. It was while driving across New Jersey that I presented to her my first recruitment problem, and she immediately came out with the name of a man whom she regarded as the only obvious candidate--namely, J. Edward Rall,

always known to his friends as Ed. This was a man whom I did not know and indeed of whom I had never heard. He was at that time working in Memorial Hospital, New York, with the senior endocrinologist, Dr. Rulon Rawson. Upon arriving in the big city, I telephoned Ed and made an appointment to visit with him on the following day. He has often recalled to me the nature of this first meeting. Innocent as I was in the ways of big government recruitment, I did not regale him with all the advantages of Federal service. Instead, I came to him with a scientific question. Knowing of his interest in the physiology of the thyroid, I asked him what he thought of the recent publications of Martius, in which it was claimed that the mode of action of thyroxin was to uncouple the so-called coupled oxidative phosphorylation, a phenomenon which had been developed largely by another old friend, Herman Kalckar. Martius' conclusion was based in part upon what was known of the mode of action of trinitrophenol, a toxic and explosive material which had been encountered as an industrial poison during the war years. The symptoms of its intoxication were in some regards similar to a thyroid crisis. This poison uncoupled the very tight coupling between the reactions of oxidation and those of ATP synthesis, sometimes called phosphorylation. Ed Rall apparently was surprised by my inquiry but it did lead to an enlightening and lively discussion based upon which I knew that I had my man. I offered Ed a position as chief of the clinical endocrinology branch and with great promptness he accepted. I believe he actually arrived in Bethesda before I did. It proved to be a remarkably successful recruitment. Ed Rall and the NIH were made for each other. He is a man of great charm and warmth and much scientific acumen. He developed a lively group of colleagues all interested in one or another phase of thyroid physiology, and we have remained close friends over the ensuing years. His delightful wife, Caroline, gave him strong support until she unfortunately contracted a breast cancer and, despite the best treatment that could be provided by the National Cancer Institute, ultimately died. The second Mrs. Rall, Nancy, is an intramural NIAMD scientist. When I left NIH in 1962, Ed Rall was named to succeed me as scientific director of the National Institute of Arthritis and Metabolic Diseases, a choice which I heartily

*This institute has since had its name changed, first to National Institute of Arthritis, Metabolism, and Digestive Diseases and more recently to National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases. These ill-advised changes were made in response to political pressures from disease-oriented lobbies.

applauded. He gave that institute excellent guidance and administration for more than 20 years. Then, in 1983, he moved to Building One to become deputy director for science, the position which I had earlier vacated.

One of the important functions of a scientific director is to be familiar with the varied and extensive scientific activities and productions of all of his laboratories and branches. To do this he must try to read each manuscript, or at least its summary, before it is submitted for publication; and, indeed, he is deputized by the Director, NIH, to approve such publication. During my tenure I made a conscious effort to perform this function although many of the papers submitted to me were quite beyond my scope to understand or to criticize. Only occasionally would I red-pencil a manuscript when it passed over my desk. In fact, I can recall only one occasion and this was a paper from the laboratory of my friend Gordy Tomkins. The paper dealt with the isolation and properties of the enzyme glutamic dehydrogenase derived from rabbit liver. Gordy was concerned with the state of polymerization of this enzyme and its changing activities. The contents of the manuscript appeared to be of the highest quality and it was only when I encountered the "conclusions" that I received a shock. Here I read, "The livers of 24 rabbis . . ." Clearly this was not to be condoned, and I wrote in red pencil "Discriminatory" across the page and sent the manuscript back to Gordy, suggesting that the last page be retyped. One of my duties as scientific director was to compose an annual report of the scientific activities of the intramural program. This, like so much else at NIH, was done in a hierarchical fashion. Each bench scientist composed a few paragraphs describing what he or she did. These were melded by the section chief, and the reports of the section chiefs were assembled by the laboratory and branch chiefs. These in turn were presented to me for the final composition. My first year at NIAMD I was advised that a strong annual report was a very important document, that it would be studied by all those above me, and that my success or failure in the competition for future funding would be determined by the strength or weakness of my annual report. I therefore devoted a great deal of time to assimilating all the information that my laboratory and branch chiefs provided to me. I tried to show how activities in one laboratory affected those in another laboratory. I sought evidence of effective collaboration and complementation among our several programs. Indeed, I believe I spent every evening and weekend for a period of about three months putting together my final document which was quite lengthy. This was then

typed and submitted to the director of the institute and by him, in turn, to the Director, NIH. I heard nothing further concerning my submission over the many months that followed and was not a little disturbed, since I felt that my valiant effort really deserved better treatment. Then the ensuing summer I had occasion to call on Dr. Cassius Van Slyke, then the deputy director of NIH. At that time Building One had no air conditioning, and since the day was hot, Van Slyke had propped his office door open. I looked down at the floor and saw that it was my fat and ponderous annual report that was keeping the door from swinging closed. Noting the use to which it had been put, I vowed to myself that in the future I would provide an annual report with an absolute minimum of labor. In the years that followed this is precisely what I did. I simply strung together the contributions of the laboratory and branch chiefs, an activity that took no more than an hour or two, and submitted the result to my superiors. These, I felt certain, would serve adequately as door stops. I vividly recall the very first meeting of the scientific directors that I attended in Building One under Jim Shannon's chairmanship. There were two items on the agenda for discussion that day. The first of these had to do with the propriety of charging the cost of the white trousers, which some of the organic chemists liked to wear in the laboratory, to the Federal account. The law said something about the provision of uniforms to employees where these were indicated and necessary, and the question was: Were white duck trousers an appropriate uniform for organic chemists? The matter was exhaustively discussed. Every conceivable analogy was raised in an attempt to determine the nature of "an appropriate uniform." The question was left unresolved. The second topic on the agenda had to do with details of construction of the Clinical Center. This is a very large building, having approximately 3,000 doors. In order to reduce the task of the night watchman who was required to make several trips every night looking into every room, each door was provided with a large glass panel so that he did not have to unlock and relock every door in the course of his fire rounds. Some of the scientists objected. Often the very scientists who figured out ways of defeating the door closure devices, and who propped their doors open so as not to feel too confined, were the ones who objected most strenuously to the transparent windows in the doors. It gave them the sensation of a goldfish in a fish tank. They could be scrutinized by everyone who chanced to pass down the long corridors. In order to relieve themselves of this goldfish neurosis, many occupants had covered the glass

panel with metabolic charts, blotting paper, aluminum foil, or any other opaque material, much to the irritation of the night watchman. The order had therefore gone out from the Director of the Clinical Center, the very competent Dr. Jack Masur, that the windows had to be left unobstructed. However, many persons seemed to have more defensible reasons for wishing privacy in their offices. This was particularly true of the clinicians who used their offices often for confidential meetings with patients and with the families of patients. Such interviews are certainly favored by a modicum of privacy. Various solutions to this quandary were suggested. Frosted glass might be inserted in some of the doors. Some of the windows could be protected by window shades that could be used temporarily to assure privacy and which could then be raised at night to provide a view for the night watchman. Again this matter was exhaustively discussed by the scientific directors, the entire meeting lasting perhaps four hours. No solution was found.

Immediately after this meeting, I called Marney and said that we had made a mistake coming to Bethesda and perhaps we should consider a return to the PHRI. Of course we did not, and subsequent meetings of the scientific directors turned out often to be far more substantive. However, trivial questions continued to recur and to be debated endlessly. At that time the principal of triviality enunciated by Parkinson still lay in the future.

My last recruit to the NIAMD was Dr. Elizabeth Neufeld, who was trained in the chemistry of the plant polysaccharides by W. Z. Hassid at Berkeley. She was very highly recommended by her old schoolmate, Victor Ginsburg, who was already in the NIAMD, and I found her achievements to be impressive. Our executive officer at that time was Gil Bayliss, an old government hand but with no science in his background. He objected to the recruitment of someone in Liz's specialty as not being in the mainstream of our mission. However, I was able to override his objections and Liz joined our institute to the delight of all of the scientists. She has since shifted her field of interest into a very clinical area--namely, the understanding of that group of genetically transmitted diseases sometimes called the mucopolysaccharide storage disorders. Her work has been consistently brilliant and she has collected many important prizes. She is one of our most vigorous investigators, is held in high esteem by many postdoctoral fellows, and is in addition a lovely person.

Among the laboratory and branch chiefs with whom I had to deal, perhaps the most distinguished was Ralph Lillie. He devoted his research efforts to the

application of microscopy to all of the color reactions that he could discover in the realm of organic chemistry and was remarkably successful at this particular activity. He was very much my senior and claimed to be the last commissioned officer in the Public Health Service to possess a sword. Shortly after I arrived I learned that he was playing host at an international congress of histochemistry which was being held at one of the hotels in Washington. I learned that in those days of the McCarthy era there was a curious rule which required clearance by the FBI before anyone could attend an international congress, even one held in Washington. Since Ralph had allowed his own security clearance to lapse, we were informed that he could not participate in this meeting. He was, of course, outraged. We moved heaven and earth and managed to secure the necessary clearance in a few days instead of the usual several weeks or months. Ralph Lillie used to attend our seminars in the section on intermediary metabolism and was always welcome. His interests were very wide and his knowledge great. He developed a series of retinal detachments, a very serious catastrophe in the career of a professional histopathologist, and finally took a disability retirement. After leaving NIH, however, he continued to serve at Tulane Medical School as professor of pathology for many years.

The most ebullient laboratory chief in the institute was surely Fred Brackett. He had rosy cheeks, a shock of white hair, and the loudest laugh in seven counties. He found life and science vastly entertaining. He started life as a physicist in California and spent a summer while a graduate student at Mt. Wilson Observatory. While there he studied the solar spectral emission and discovered the series of lines in the hydrogen spectrum known forever after as the Brackett series. This all happened in the early 1920s. About 50 years later, NASA procured the first photographs of the far side of the moon and, in accordance with well-established precedent, proceeded to name each new crater after a dead astronomer. They apparently ran out of obvious names and therefore attached the name of Brackett to one of the craters. They erred in two regards. Fred Brackett was probably not an astronomer and was most certainly not dead. He was in fact living near the NIH, having retired from his position as chief of the laboratory of physical biology. We gave him a champagne party to celebrate the only living scientist with his name on the moon.

Lyndon Small was the director of the laboratory of chemistry. He was our senior organic chemist on the campus and the world's leading authority on the structure of the morphine alkaloids. He was a chemist of the old school who

liked to run his organic chemical reactions in kilogram lots. As a result, we had in our laboratories substantial quantities of morphine and its many narcotic derivatives. This posed a peculiar problem to the administration of NIAMD when Lyndon Small died. Fear of theft of these large amounts of narcotic drugs commanding a very high street value led to problems in their safekeeping, which were assumed by his successor, Dr. Bernhard Witkop. Witkop's interests, it may be noted, were not in narcotics but chiefly in poisons. He had done important work prior to coming to NIH on the structures of poisonous materials in the deadly mushroom Amanita phalloides, and after coming here he became interested in the poisonous materials in certain frogs of South America. He is a remarkably scholarly man who is strikingly polylingual. He can speak readily in French, German, Italian, and Schweizerdeutsch and has developed great facility in Japanese, a language which he has learned from his many Japanese post-doctoral fellows and which he has practiced on his several voyages to Japan. The head of our laboratory of pharmacology was Sanford Rosenthal, a quiet and persevering scientist who had early in his career developed dyes for the diagnostic tests of liver and gallbladder function. By the time I arrived at NIH he was deeply engrossed in a novel approach to the treatment of burns. This soon resolved itself into the oral administration of a slightly alkaline solution of sodium chloride, and he determined that this quite simple treatment was approximately as effective as the intravenous administration of plasma and other fluids. In order clinically to test this laboratory observation, he had to find a country in which burns were both frequent and poorly treated. Such a country turned out to be Peru, where many natives lived in highly combustible houses. Sanford spent several years in and out of Peru setting up a program for the testing of the oral saline therapy that has finally become accepted therapy, particularly in catastrophe situations where sophisticated medical procedures may be impossible or difficult to carry out. Rosenthal has been succeeded as chief of his laboratory by our good friend and neighbor, Herbert Tabor. The Tabors have four children of ages roughly comparable to those of our children, and as a result the association between Stettens and Tabors extends through two generations and even somewhat into the third. Herb has for many years served as editor of the Journal of Biological Chemistry, which is certainly one of our most prestigious journals. The Tabors work closely together in the laboratory and are a splendid example of marital cooperation in

all aspects of their lives. They clearly demonstrate that fear of nepotism is not well grounded in our profession.

While serving as scientific director of NIAMD, I was in daily contact with Joe Bunim, the clinical director. When we were together at Bellevue Hospital, Joe was already deeply involved in the study of arthritis. He had been recruited to NIAMD before I had and indeed he participated in recruiting me. We had adjoining offices on the 9th floor of the Clinical Center, separated only by a module filled with secretaries. Even in our domestic arrangements we were neighbors. The Bunims with their three children and the Stettens with their four lived in adjoining houses of virtually identical design on Maple Avenue, Chevy Chase. It followed that Marney and I saw a good deal of Joe and Miriam Bunim, and our oldest daughters were on friendly terms with the Bunim kids.

Joe was a serious and studious man, enormously well informed on all aspects of the rheumatic diseases, and--what was relatively rare at the NIH--a truly dedicated clinician. In the course of my work I walked up and down the long corridor of the 9th floor many times each day, passing in front of Joe's office. If, as sometimes happened, I had a lame back and walked stiffly, Joe would immediately notice this and come popping out of his office to inquire what was the matter. He was an enthusiastic therapist and happily advised my mother in the management of her osteoarthritis and Paget's disease, Marney in the management of a subdeltoid bursitis, and me with my occasional lame back. He was one of the very effective Clinical Directors and ran a medical service that was a model of propriety. He was interested in all of the so-called collagen diseases but particularly in rheumatoid disease. He originally was an advocate of the then novel treatment introduced by Hensch using corticosteroids. When new drugs of this series, such as Prednisone and Prednisolene, became available for testing from Merck, it was natural that the major clinical tests should be run by Joe Bunim on patients in the Clinical Center.

A curious episode occurred one day when all of the orderlies who normally distributed the food trays were summoned to a meeting. Joe came to my office very distressed because the nursing staff refused to distribute the trays, stating that this activity was not in their job descriptions. Since many of the patients were participants in metabolic studies, it was important that they be fed on schedule. I proposed that Joe and I distribute the trays, confident that the nurses, upon seeing our action, would join in. Regrettably they did

not. I still have a vivid picture of our charge nurse, arms crossed over her bosom, eying us balefully down the corridor. I was shocked at what I regarded as lack of common humanity in the profession of Florence Nightingale. I continue to be shocked when I read of representatives of the health professions employing the strike as a means of settling their disputes.

Joe Bunim was a prodigious worker. Shortly after I left Bethesda for New Brunswick, Joe had a myocardial infarct while at home alone. He opted to drive himself to the Clinical Center where he was admitted in very serious condition. He died at the Clinical Center shortly thereafter.

Probably the best known group of investigators in the NIAMD had been collected by Arthur Kornberg. He had left NIAMD for Washington University, St. Louis, by the time I arrived but the remainder of his group included Bernard Horecker, Leon Heppel, Herman Kalckar, Gilbert Ashwell, and William Jakoby. Arthur Kornberg had been a stern drillmaster and had established a ritual of daily lunchtime seminars which all were expected to attend. Traditionally this ritual was not interrupted even for holidays such as Thanksgiving or New Year's Day. Under the continuing guidance of the new laboratory chief, Bernard Horecker, this stern ritual continued with only minor relaxation. All of the members of the group and the postdoctoral fellows whom they attracted attended regularly. It was in this group that the major developments in enzyme chemistry on the NIH campus took place.

An event important to me during these years occurred under the term of the Lacy-Zaroubin agreement, a series of exchange missions in medical sciences undertaken between the Soviet Union and the United States. I was selected to assemble the American group of endocrinologists who were to visit the Soviet Union according to the terms of this exchange. This news caught up with me while I was driving with my family across the United States in the summer of 1958 to attend a month-long meeting on physical biology at Boulder, Colorado, put together by Francis Schmitt of MIT. The dormitories of the university were placed at the disposal of this meeting and we had a very enjoyable and stimulating time. Immediately upon my return to Bethesda, I started collecting names of other possible participants in our proposed Soviet junket. I was advised that it would be desirable to have at least one member of the team who was fluent in Russian and this clearly and sharply pinpointed Rachmiel Levine, an established authority in diabetes on the faculty of the University of Chicago. He had been born in the Ukraine and agreed to polish up his Russian

language during the months immediately ahead. Others who participated in the tour were Edwin (Ted) Astwood, Dwight Ingle, and Ed Rall--my friend and colleague from the arthritis institute. Ted was a pituitary physiologist and clinical endocrinologist at Tufts Medical School in Boston. Dwight Ingle, an old friend and collaborator whose interests were chiefly in the hormones of the adrenal cortex, was at this time at the Upjohn Company, Kalamazoo, Michigan, but was soon to move to the University of Chicago's Physiology Department.

We were provided with extensive briefings at the State Department and, be it whispered, at the CIA. The purpose of the latter briefings seemed to be chiefly to acquaint us with the names and faces of the scientists whom we might encounter. To this end they reviewed many photographs of biomedical scientists in the Soviet Union and encouraged us to collect more such portraits for their rogues' gallery. They provided us with virtually unlimited film for our cameras in order to facilitate this task and we all merrily took pictures throughout our tour. They told us that in each mission from the USSR there was one member who was clearly not a scientist, and they wished better to identify possible representatives of the Russian secret police. Rachmiel, who always planned carefully, purchased a fine new 35mm camera immediately before departing the United States. He neglected to test the camera, and it was only after our return that he discovered that the shutter was defective and that it apparently never once opened during all of our trip through the Soviet Union. He had snapped many scenes but found only unexposed film on his return. My snapshots turned out well and I gave him a set.

We were advised to keep a careful journal of our seeings and doings and to this end we were provided with a dictating machine. We were also advised as to the kinds of gifts that we could appropriately bring to our Soviet hosts, such as phonograph records, current news magazines and, for the children, chewing gum.

In May 1959, we flew from Washington, via Boston and Shannon, Ireland, to the London airport, where all our luggage was lost. We were about to enter an unfamiliar country with nothing but the clothes on our backs. We were advised to proceed to Copenhagen, and fortunately it was there that our luggage caught up with us. Thence on to Moscow, where we were met by an impressive contingent from Moscow scientific institutes and from the American Embassy. On this and on several occasions the greeting included a ceremonial delivery of large bunches of peculiarly thorny roses to each of us which, together with our

satchels and raincoats, we had to dispose of as best we could. We were put up at the Ukraine Hotel, a modern building of the Stalin style of architecture--tall, overly decorated, very symmetrical, with great expenditure of materials and labor in the public rooms and rather ugly individual bedrooms. Although modern, the plumbing always seemed to be defective. This was a characteristic of each Russian hotel in which we stopped and we spent some time repairing plumbing.

I recall that on our first night in Moscow we were entertained at the Israeli Embassy where the tenth anniversary of the founding of Israel was being celebrated. The invitation may have resulted from the fact that the Israeli Ambassador to Moscow chanced to be an endocrinologist. The following day we were briefed at the Soviet Academy of Medical Sciences and were told which cities and institutes we would be allowed to visit. Certain cities at that time were definitely not accessible to American visitors. We were again advised that we might photograph anything except airports, railroad installations, military installations, and hydroelectric plants. We furthermore were assigned a guide, Valoydia (nickname for Vladimir), who was a law student unusually gifted in English. He was to accompany us everywhere and facilitate our travel. When we lectured, as we were invited to do at several institutes, Valoydia would act as interpreter. This often seemed unnecessary, for when Valoydia could not come up with the proper Russian translation of a word, several voices in the audience would produce the needed term. Most Russian scientists were quite literate in English and many spoke it quite well.

Our tour started with Leningrad. We traveled there on Russia's most famous train, the Red Star Express, which made a non-stop overnight run on what was purportedly the longest perfectly straight piece of track in the world. What we did not appreciate was that the train was energized by soft coal. Ed Rall and I shared a sleeping compartment and thoughtlessly left the window open, only to find in the morning that we were both coated with a thin and uniform layer of dark brown fly ash. As we were scraping this off of ourselves, I walked the lady conductor with the samovar of tea to start our day.

We were met at the Leningrad railroad station by the usual contingent of professors accompanied by pretty female technicians each offering a bunch of roses to us. They escorted us to our hotel which had a name that struck me as unexpected, the Astoria. I remember recounting to Valoydia the "capitalist-monopolist" activities of John Jacob Astor of New York. This hotel was a fine

old structure reminiscent of the Plaza in New York. In Leningrad we visited the Institute of Gynecology, headed by Baranov who had been a member of the Soviet reciprocal team which had visited each of us in the United States. Baranov and his physician wife were deeply in love with their city of Leningrad. I believe they were Leningraders first and Soviet citizens second. Leningrad, in contrast to Moscow, proved to be a truly beautiful city. We saw many of its fine churches, now called anti-religious museums. We noted particularly the restorative work that was going on at St. Isaac's Cathedral with its fine gilded dome, and were taken through the Winter Palace with its remarkable collection of works of art, particularly of French impressionist painters. We also made an expedition to the suburbs to visit the laboratories of Ivan Petrovich Pavlov where research on the dog continues. It was of particular interest to see the equipment that Pavlov himself had used, such as the wooden frame for restraining the dog while saliva was being collected. We saw antiquated equipment identical to this in many of the research laboratories that we subsequently visited. The remainder of our travel was entirely by air. We spent time in Kharkov, Kiev, Sukhumi, and finally returned to Moscow. In each of these cities we visited one or more scientific research institution of considerable interest. Perhaps the most unusual was the baboon colony in Sukhumi. This town at the northeast corner of the Black Sea, at the foot of the Caucasus Mountains, is the capital of a republic named Abkhazia, with a language and a script all its own. It has a semi-tropical climate and has been a resort town for many, many years. It is the supposed site of the Greek city of Colchis, the destination of Jason and his Argonauts searching for the Golden Fleece so many years ago. But earthquakes have apparently dumped all the Greek structures to the floor of the Black Sea and nothing visible remains. The city itself is remarkably similar in mood and in appearance to towns of the French and Italian Riviera. Whitewashed stucco hotels line the parade which follows the shoreline. Little outdoor cafes decorate this main street and naval and military bands march up and down playing music. Some years earlier, under the governance of Lenin who leaned heavily upon Pavlov for advice in such matters, a major colony of baboons had been established. By the time we visited, this colony was self-sustaining. No more imports were required. The baboons bred freely in the large outdoor pens in which they were restrained by tall concrete walls, and the total population at that time was said to be about 1,500. Any Soviet scientist wishing to perform experiments upon baboons could secure

assignment to this center which contained, in addition to the animals, adequate laboratory buildings. It was here that we were told of experiments that appeared to me to be among the more interesting activities that we witnessed. Its director was a man named Yutkin and his interest was in the etiology of hypertension. The typical experiment which he performed was based upon the curious structure of the baboon colonies. Each colony of baboons had one bull, who was easily identified. He was surrounded by a harem of females, many of whom were accompanied by their pups that they kept track of by holding their tails much as a dog owner holds a leash. Around the periphery of the colony were the bachelors. If the bull were placed in a cage within full sight of the colony, the many bachelors would at once get into a battle and sooner or later one would be victorious and assume the leadership of the harem. The former bull, witnessing this from behind bars, would over the ensuing two weeks develop an irreversible hypertension and would within two years die a typical hypertensive death either from stroke or from heart or renal failure. Thus a "frustration-hypertension" could be generated in these animals without the use of pharmaceutical or surgical procedures.

At each city that we visited we were given a banquet. These were always sumptuous and hospitable but none exceeded the banquet that we were given at Sukhumi. A fine restaurant upon a hilltop was selected for this purpose and the Abkhazian Medical Society was our host. I recall that the man assigned to converse with me was a practitioner of medicine in a village in the Caucasus Mountains. I inquired of him as to the truth or falsity of the stories he had always heard of the extraordinary longevity of the natives of this mountain range, and he indicated that he had in his practice a number of individuals said to be in excess of 100 years of age. He believed, however, that their longevity was probably chiefly genetic rather than nutritional or environmental, as they all belonged to one or two families in one town. Since birth records from 100 years ago were not available, the exact age of these individuals was subject to some uncertainty.

Our general impressions of biomedical research in the Soviet Union in 1939 were that they were far behind us and had relatively little chance of catching up in the next generation. They were still suffering from the adverse effects of Lysenkoism, and although Lysenko was no longer in power, a whole generation of genetic research had passed them by. We visited two medical schools and noted the very large proportion of women students. The teaching included

material which had not been taught in the United States in two generations. Thus the pharmacology was almost entirely materia medica. Of their several research interests, one in which they seemed particularly concerned was transplant surgery, and we were told of experiments in which the head of a dog had been successfully transplanted. We were never shown the dog.

In 1962, Floyd Daft, with whom I had excellent relations, decided to retire and the directorship of NIAMD passed to Donald Whedon who was a clinical investigator in the institute. At about this time I was considering accepting an offer to become the dean of a yet-to-be-founded medical school at Rutgers University. The prospect of building a medical school all my own was overwhelmingly tempting. Rutgers, furthermore, was Marney's home college, she having graduated from the New Jersey College for Women that was now Douglass College of Rutgers University. We looked at this job offer as carefully as we could, recognizing that we were entering unfamiliar soil. Clearly a major factor in determining my acceptance of the offered position was the President of Rutgers, Mason W. Gross, one of the few truly great men with whom I have had contact. We found ourselves in agreement as to the kind of a medical school that had to be built on the campus of his beloved Rutgers University. And so once again, in 1962 Marney and I packed up our family and possessions and moved to the banks of the old Raritan.

Chapter X

NANTUCKET AND WOODS HOLE

In 1957 the Stetten family spent its first summer in Woods Hole, Massachusetts, and almost every summer thereafter we have returned. Woods Hole is separated from Nantucket by bodies of water called Vineyard Sound and Nantucket Sound, and in a sense my move to Woods Hole was a return to an important scene of my youth. I had spent many lively summer vacations on Nantucket as a guest in the home of my uncle, Morris L. Ernst, and his family. In this chapter I want to present some of my friends and experiences in that region.

All my life I had an unusually close association with Morris Ernst, my mother's brother and a prominent civil liberties attorney in New York City. After the death of his first wife, Susan, around 1920, we saw much of him and his infant daughter Connie at our home. Soon he married his second wife, Margaret, a newspaper reporter on the New Orleans Times-Picayune, a woman of great wit and warmth. They, in turn, had two children--Roger, now retired from the Federal AID program, and Joan, who has adjusted remarkably well to total deafness all of her life and gradual impairment of vision in recent years.

Morris was a brilliant and energetic man who seemed always to derive intense enjoyment from whatever he was doing at the moment. Very early he was seduced by Roger Baldwin into the then new Civil Liberties Union. Together with Arthur Garfield Hayes, he shared the legal burdens of that liberal organization, becoming particularly concerned with cases involving censorship. Perhaps his best known achievement was the successful defense of James Joyce's *Ulysses* in behalf of the Random House Press. He succeeded in persuading the court that this was a work of literature, not of pornography. Having made a deal with the president of the publishing house, Bennett Cerf, that in lieu of a fee he would accept a share of the royalties on the book, he continued to derive monetary benefits from this success for the rest of his life. He served as attorney to many literary and political figures, advising them in censorship problems. He assisted Heywood Broun in the creation of the Newspaper Guild, and he became a peripheral member of the group of New York literati who convened at the Hotel Algonquin for so many years. Alex Woollcott, Dorothy Parker, and Edna St. Vincent Millay were frequent visitors at his home, an old brownstone

private dwelling on West 11th Street in Manhattan. Norman Thomas, the perennial Socialist candidate for the presidency of the United States, was often to be seen there, and Margaret Sanger, the early proponent of birth control, leaned heavily on Morris Ernst both for moral and for legal support. All in all, 46 West 11th Street was an interesting house for a growing youngster to visit. The mood was informal, hospitality was warm, and arguments were lively. Morris was inclined to settle these by reference to authority, and his two favorites were Oliver Wendell Holmes, Jr., and Louis Brandeis. Reference to the greats was invariably by first name, and I recall one occasion when Morris settled an argument by stating that Jimmy would never agree. "Jimmy who?" he was asked. "Jimmy Madison, of course," was the immediate response. Morris was not a profound scholar but he had an interest in everything and a remarkable aptitude in acquiring information from conversation. Every year or two he would compose another book, often with the assistance of a junior coauthor, presenting topics of interest to him. These related usually to what he referred to as "my love affair with the law." He wrote books on censorship, on civil liberties, on divorce, and on numerous other topics. None of these, I believe, was a best seller but all of them captured his easy conversational charm. Because of his interest in the law of censorship, he had many contacts with publishing houses, one of which was always ready to publish his latest volume. Morris' wife, Margaret, became librarian in a progressive neighborhood school called City and Country School. Here she developed her interest in etymology and wrote some charming books about the origins of words. Humorous illustrations were contributed by a friend, James Thurber.

Morris was a member of an active and successful law firm--Greenbaum, Wolff, and Ernst. He managed to persuade his partners to perform all of the drearier labors of a law firm, and he devoted himself to the more flamboyant and more newsworthy cases. Part of his arrangement with his partners was that they would mind the store while he and his family took long vacations on Nantucket Island. Shortly after his second marriage, Morris and Margaret built a handsome summer home at Monomoy Beach facing the entrance to Nantucket Harbor, with two wings, one for the children and one for the domestics, and here they went every summer. Morris soon became involved in the sailing activities of the summer colony and acquired one of the small boats with brightly colored sails referred to as the "rainbow fleet." His initial lack of navigational skills led, if I remember correctly, to calling his first boat "The Menace," but he

soon graduated to a far more seaworthy vessel. This was a handsome 37-foot ketch designed and built by John Alden of Boston. He kept it at City Island, New York, during the winters and sailed out of Nantucket during the summers. The boat was solidly built and very well equipped for cruising, accommodating easily a crew of five or six. To sail her comfortably required at least three hands, and so it was that I was invited on many occasions to take a berth as a foremast hand and sail with my uncle Morris, my cousin Roger, and possibly one or two others from City Island to Nantucket. This we would do usually over a period of four or five days, sailing by daylight and seeking a safe harbor on Long Island Sound each night. This boat, aptly named "Episode," convinced me of the beauties of coastwise cruising. Sailboat racing has never interested me, perhaps because I am not competitive by nature but also because racing appears to me to be antithetical to the greatest pleasure of sailing which is the freedom from the constraint of time. Cruising with Morris was always an adventure. Following Murphy's well-known law, everything that could go wrong with a sailboat did. On one occasion the main halyard broke and the heavy mainsail came tumbling into the cockpit with no practical means of hoisting it again. On another occasion the propeller and its shaft dropped out of the bushing through which it penetrated the hull, and seawater started pouring into the cabin. On several occasions we ran around and once we were hung up on well-marked rocks outside of Portland Harbor. All these and countless other crises Morris encountered with unshakable cheerfulness. In addition, there were minor crises. In Episode, refrigeration was by means of an ice chest. This box was equipped with a spigot to drain the water which accumulated as the ice melted; however, we frequently forgot to perform this function. As a result, our stored supply of canned foods swam in a pool of cold water. Since in those times the glue used by canners to affix labels to tin cans was water soluble, labels would soon become detached and one had no way of knowing for certain what a particular can contained. Meals were often prepared by selecting three unlabeled cans at random and mixing their contents. The results were sometimes awful to behold and worse to taste.

Nantucket was and still is a delightful island. It lies well out to sea-- that is, out of sight of the mainland--which adds to the excitement of navigation. When not approached by sail, it could at that time be reached by steamer from New York. One left New York on the New Bedford Line in the late afternoon and sailed up Long Island Sound. One then retired to a comfortable stateroom

and awoke at 7 in the morning at New Bedford, Massachusetts. You merely walked across the pier and boarded the smaller vessel that went via Woods Hole to Nantucket. It was a charming mode of travel, certainly more pleasant than going by rail from New York to Woods Hole, or driving the always monotonous Connecticut Turnpike. Nantucket, with its romantic history, its unusual collection of inhabitants, and its interesting architecture, remains in my estimation one of the most attractive places that I have ever visited. Certainly the pleasant associations which I have with the island stem largely from the hospitality and affection of Morris and Margaret Ernst.

The Ernsts were served for many years by a trio of Irish women, all related to each other, who took care of all household tasks. They entered into the family's activities to an unusual degree. Thus, when the family and their guests returned from an extended stay on the beach, the Irish maids would slap Noxzema ointment on the faces of family and guests alike while serving them food and drink. Morris held this domestic staff in very high esteem, and on one or more occasions he shipped all three of them back to Ireland so that they might visit with their relatives.

Once each summer, Morris would sail his boat to Monomoy, Cape Cod, to pay his respects to his idol--Justice Louis Brandeis. Many years before, Brandeis had authored a book entitled The Curse of Bigness in which he analyzed America's largest corporations and demonstrated that for each type of institution there was an optimal size. If this optimum were exceeded, the institution suffered in one or more ways. Its efficiency declined, its profits dropped, its stability became less assured. Morris became devoted to this concept and himself wrote a book which he called Too Big, a title suggested by a popular novel, So Big, by his friend and client, Edna Ferber, in which he developed further examples of the same phenomenon. In my own experience I have found other examples. Thus I have no doubt that there is an optimal size for a medical school student body which, if exceeded, leads to a decline in the quality of medical education.

Although I saw somewhat less of Morris and his family in later years, he continued to live an active and creative life. He defended a variety of civil liberties causes which involved him with some unsavory political figures, including Mayor Hague of Jersey City whom he attacked, and Dictator Trujillo of the Dominican Republic, whom he unexpectedly defended. He was an occasional guest at the White House during Franklin Roosevelt's presidency and continued

to correspond with and advise the incumbent at 1600 Pennsylvania Avenue through the Nixon administration.

After vacationing in various resort areas of the New England mountains and the Atlantic coast, we finally decided that we could best spend our summers in Woods Hole. A number of our friends had already developed the habit of visiting this center of biological research each summer and it was Giulio Cantoni and Andrew Szent-Gyorgyi who convinced us to give it a try. In 1957 we rented a handsome old house in full view of Buzzard's Bay and moved in with our family of four young children and a resident housekeeper. The summer was a great success. Marney and I attended the daily morning lectures in the physiology course as well as the regular Friday evening lectures at the Marine Biological Laboratory. The children were entered in the appropriate classes of the Children's School of Science, an institution which distinguishes Woods Hole from all other resort areas. It was apparently an invention of the wives of some of the summer scientists many years earlier, a device which exploited the educational opportunities of the environment and at the same time got the kids out of the house for a few hours every day. We rented laboratory space in the Marine Biological Laboratory and carried out a few experiments in the area of carbohydrate metabolism and its endocrine regulation in mollusks and crustacea. Whereas many research activities are difficult to carry out in Woods Hole, the availability of marine invertebrates has made it a popular center for biologists, particularly during the summer months.

The following summer we all participated in a memorable month-long meeting on physical biology held on the campus of the University of Colorado at Boulder. We combined attending this meeting with an extended tour across the country to California, sometimes camping out overnight, particularly in the national parks. The next year, 1959, we were once again ready for Woods Hole. We took a trip there during the early spring to explore home rental opportunities and ended by purchasing a house at 6 Brooks Road, which has been our summer home ever since. Although originally a modest summer house, we have since expanded it markedly, winterized it, and consider it as a possible place of ultimate retirement. This particular sequence of events, by the way--namely, purchase of a summer home, winterization, and retirement--is a not infrequent pattern among our circle at Woods Hole. We have made many friends there. Our children all took courses at the Children's School of Science for up to eight years, and two of them after graduation served as assistant

instructors. Here on Stony Beach they all learned to swim, and here they all took sailing lessons.

With our house we acquired the sailboat belonging to the former owner. It was a Cape Cod knockabout, an 18 1/2 foot centerboard sloop, which was the most popular racing class out of Woods Hole Yacht Club. Mostly we used this boat as a day sailer, although Gail and some of her friends occasionally entered it in the club races. The boat was of wooden construction, with canvas sails, and in frequent need of attention. In addition, my earlier exposure to coastwise cruising left me less than satisfied with this open boat. I therefore subscribed to Yachting magazine and religiously studied all the photographs, the plans of sailboats, and particularly the advertisements. Marney and I took to going to the annual boat shows and visiting shipyards and yacht basins. I was very much taken with the Westerly line of twin-keel sloops but was deterred by their relatively high price. We then saw the American version of this British yacht, the Tylercraft 24. Mr. Tyler managed to fit into this small hull bunks for four, a small galley, an ice chest, and a head. The cockpit was ample and by means of a trick lift in the cabin roof full standing head room was provided. We ordered this fiberglass boat and took delivery in the summer of 1966.

The naming of a new boat calls for a family council and there was much discussion. Finally we agreed to call the boat Taladma, after a soft-hearted flying beast in one of our favorite fairy tales, The Enchanted Forest, by Mary Raymond Shipman Andrews. It may be recalled that the reason for Taladma's dolorous state was that she had lost her tail tassel during one of her many flights. Our elegant little Dyer dhow which we towed behind was therefore named Tail Tassel. We set down our mooring in Great Barbor at the infinitesimal Woods Hole Yacht Club. Marney and I were now ready to cruise among the small harbors on or near Cape Cod on our own, and this we found romantic and exciting. At least two of our four children, Gail and George, enjoyed sharing in this exhilarating pastime.

Because Vineyard Sound and Buzzard's Bay, the two bodies of water which are connected by the strait called Woods Hole, have tide cycles which are out of phase, the currents which run through the Hole are tricky and swift. The success or failure of any projected sailing trip is therefore critically determined by the attention which is paid to the tide and current tables. Fortunately, these are analyzed in detail in a yellow-bound annual paperback

familiarly known as Eldredge's Tables, a volume which is carefully studied by all cautious sailors in these waters. Fairly early in our cruising career, after much study of these tables, we selected the ideal day and time to sail from Woods Hole to Nantucket. The course from Nobska Light, our own particular lighthouse, to the jetties of Nantucket Harbor is magnetic southeast. Allowances must of course be made for the lateral thrust of both wind and current. Apparently we did these things correctly because about six hours after leaving Woods Hole we entered Nantucket Harbor in high spirits. There is on this sail a brief period when the mainland has dropped below the horizon and the island has not yet come into view. The landfall is therefore of deep significance to the navigator. Marney, George, and I moored Taladma close to Morris Ernst's dock, and feeling a little bit like Christopher Columbus we went ashore to spend several days with the Ernst family. On the return trip, we had Roger Ernst and his son aboard. Much of this passage was sailed in dense fog but no serious problems were encountered.

Emboldened by the success of this voyage, we made subsequent short cruises, often spending the night at anchor in such harbors as Cutty Hunk, Menemsha, or Pocasset. At least once each season we would visit Tarpaulin Cove on Nauahon Island and Lake Tashmoo on Martha's Vineyard. Our longest cruise was a visit to Cohaaset, a rocky harbor just south of Boston. We were impelled to go there because Mary was spending the summer as an apprentice in the musical theatre there. She was given a singing role in the musical comedy "Oliver," and this we had to see. To get to Cohasset, an hour and a half trip by car, it was necessary to sail the entire length of Buzzard's Bay, through the Cape Cod Canal, and then across a considerable stretch of Cape Cod Bay and into Massachusetts Bay. We took two days in each direction for this trip. As we were finding our way through the rocky entrance of Cohasset Harbor, Marney was reading aloud to us from Thoreau's account of his tour of Cape Cod. She had just come to the passage which described in gruesome detail a terrible shipwreck which had occurred the day of his visit to Cohaaset more than a century earlier. The bodies of large numbers of Irish indentured servant maids were swept into the harbor and were buried, with his participation, in a common grave. We saw Mary's production that night and the following morning found ourselves fogbound in port. Local sailors advised against our trying to find our way out of this difficult harbor with poor visibility, and we therefore

stayed for an extra day in Coahaaset. This gave us the opportunity to seek out the common grave which Thoreau had helped to dig.

We thoroughly enjoyed Taladma. She was a boat with many desirable characteristics. Her twin keels gave her great stability, combined with shoal draft (two feet). Furthermore, when she ran aground, as she did occasionally, because of the twin keels she remained upright. She was sturdy and took in no water whatsoever. A well was provided behind the cockpit which accommodated a small outboard motor sufficient to drive her at four knots. But it was a matter of pride to use the motor as infrequently as possible. One filling of the 5-gallon tank was often enough for a summer of sailing. One feature which we provided was a roller reefing genoa jib. This sail was my pride and joy. It was delightful when coming up to the mooring to haul on the proper line and see this large foresail roll up on its luff-line like an old-fashioned window shade and essentially disappear. Immediately the boat would lose way so that picking up the mooring was usually quite easy. During one season, George used Taladma as a private apartment, sleeping aboard almost every night while she rode at anchor off Woods Hole Yacht Club.

Maintenance of Taladma did not involve much effort. Each year she received one coat of antifouling paint below the water line and the usual minor repairs of her brightwork and rigging. However, I was beginning to suffer from impaired vision. At first I was unable to read the compass and charts, then I found that I could not see the buoys and other markers, and finally I was unable to see approaching vessels. At this point I knew that I could no longer navigate. The rest of the family was insufficiently moved to go through the labor of putting the boat into the water. After she had sat for two seasons on her trailer in our backyard at Woods Hole, I determined that the time had come to dispose of Taladma. Finally, in 1979, we sold her to a colleague, James Sidbury, scientific director of the National Institute of Child Health and Human Development. No one in the family shed any tears.

Woods Hole is a remarkable community. It houses two important ocean-related Federal agencies: an important branch of the Coast Guard and a major laboratory of the Bureau of Fisheries, Department of Interior. In addition, the town contains two independent research institutions. The larger of these is the Woods Hole Oceanographic Institution (WHOI) and the older is the Marine Biological Laboratory (MBL). It is with the last-named institution that we are chiefly associated. Nearly 100 years old, the MBL was originally established

by a number of biologists who came from Harvard, the University of Chicago, and elsewhere during the summer. Its original laboratories, although fairly primitive, attracted many of the outstanding figures in American biological science, such as Jacques Loeb and Thomas Hunt Morgan. The reason was partly the unusual variety of marine life which could readily be found in adjacent waters. More important, however, was the opportunity to associate with one's peers, teachers, and students in a relaxed and happy mood. Over the many years that we have returned to Woods Hole, we have made many and close friends. The town is of such a size that a youngster on a bicycle can command it. In fact, I believe that our children developed larger circles of acquaintance in this town than we did and several of them still consider it home.

Years before the Pilgrims landed at Plymouth Rock, Captain Gosnold is reputed to have touched at Woods Hole while exploring the coast in preparation for his bringing the Virginia Company to America. For reasons which I do not know, that company favored Jamestown over Woods Hole. The town is built around a small arm of the sea called Eel Pond, which is separated from Vineyard Sound by a narrow passage spanned by a small drawbridge, a featured attraction of our main street, called Water Street. The main buildings of the Marine Biological Laboratory back onto Eel Pond. Of recent years there has been increasing pressure to enlarge the year-round activities of MBL. The reason for this is chiefly economic, it being difficult to raise funds for an institution which is operated only three or four months out of the twelve. A perennial problem facing its director, currently Paul Cross, is the fraction of space which should be allocated to year-round occupants as compared with that which should be reserved for summer workers. This is a question contested with some warmth along Water Street and debated at the meetings of the Marine Biological Laboratory Corporation, which owns the laboratory and includes virtually everyone who has worked for two or more summers at the MBL.

The Marine Biological Laboratory contains many individual laboratory modules which are available for rent to qualified scientists. These laboratories are relatively spartan in their appointments but are distinguished by the presence of running seawater, thus facilitating studies using living marine forms. The MBL also boasts one of the oldest and finest library collections of biological journals in the United States. A prominent feature at MBL is the assortment of courses which are available in several specialties. These liven the summer season and bring hundreds of students into town. Each typical course, which

may be in physiology, in neurobiology, in embryology, in marine ecology, or in other subjects, consumes very nearly one hundred percent of the waking hours of both the students and the faculty for at least six weeks. The enthusiasm of both students and faculty is, I believe, greater than generally encountered at more staid university campuses, and the experience is often career-determining to the student. Our daughter Gail took the experimental invertebrate zoology course when she was a college biology major. Many graduates of these summer courses acquire the Woods Hole habit and manage their lives in such a way as to return regularly to this intellectual haven. Another feature of MBL during the summer is its series of regular Friday night lectures. These are given by distinguished visitors and always attract much attention. They cover virtually all aspects of biological sciences.

In addition to sailing and swimming, Woods Hole offers the usual assortment of summer diversions, including tennis, golf, and fishing, which have never attracted members of my family. It also provides access to weekly performances by the College Light Opera Company at Highfield Theatre in Falmouth. Here my children gained familiarity with the operettas of Gilbert and Sullivan, which had always been dear to me. My daughter Mary selected Oberlin as her college because of this exposure and she sang with the group for two years. Most important, it has offered to Marney and me an opportunity to come together with old friends on a continuing and intimate basis. Here each summer, until his death, I could visit with my old mentor from P & S, Bob Loeb. Here also do I find occasion to meet with Walter Schlesinger, a faculty colleague at Rutgers Medical School, and David Shemin, a friend from P & S days. Eric Ball, formerly of the physiological chemistry department of Harvard Medical School, was a perennial summer resident, as has been my fellow traveler in the Soviet Union, Rachmiel Levine. Woods Hole is the permanent residence of Albert Szent-Gyorgyi, a particularly colorful and dynamic senior member of the biochemistry fraternity, a Nobel laureate whom I had known earlier in New York. He continues to do laboratory research at the MBL.

Perhaps most important to me has been the opportunity to develop a close friendship with Philip Handler. My contacts with Phil go back quite a long way. Originally these stemmed from mutual laboratory interests. Phil had been studying the metabolism of the a-vitamin, nicotinamide. This material, at least in some species, is excreted in the urine as its N-methyl derivative. He published a study in which he fed massive doses of nicotinamide to rabbits and

noted that the animals developed fatty livers. Simultaneously and independently I had been studying the metabolism of guanidoacetic acid, which is also methylated in the animal body to form creatine, and I had found that when rats were fed large doses of guanidoacetic acid they also developed fatty livers. Clearly in both of these instances there was a loss, a hemorrhage, of methyl from the animal reservoir. At about the same time, Vincent du Vigneaud and his colleagues had characterized the methyl group as being nutritionally indispensable, usually provided in the diet as the amino acid methionine or the base choline. Charles Best, of insulin fame, had reported much earlier that rats on diets deficient in choline would develop fatty livers and that this abnormality could be prevented or cured by the administration of choline. Choline was named by him a "lipotropic" agent. It now appeared that Phil and I had independently encountered one and the same phenomenon--namely, that the addition to the diet of a reagent which gobbled up methyl groups had the same effect as choline deprivation. Since choline, which is trimethylethanol-ammonium hydroxide, is a heavily methylated compound, these findings all fitted together with satisfying elegance. Phil and I exchanged information with each other, and he invited me to Duke to present my results in a seminar. As recounted in an earlier chapter, we both participated in the composition of the textbook Principles of Biochemistry and I found him to be the most congenial of my coauthors. On at least one occasion, my family joined me on a visit to Durham which climaxed in a departmental banquet at which a whole roast pig and innumerable hush puppies were consumed.

It must have been during the year following our first summer at Woods Hole that I first learned that Lucy Handler was suffering from multiple sclerosis. I recall Phil discussing this matter with me during an automobile trip somewhere and mentioning that Lucy, like at least one other victim of this disease whom I have known, did poorly during extreme summer heat. I therefore mentioned that we had spent the previous summer at Woods Hole and found the climate very refreshing. The next summer, the Handlers joined the Stettens and since that time have been faithful summer residents in Woods Hole. After trying several homes about town, they finally purchased a large house with a magnificent view of Buzzard's Bay and a private swimming pool about two blocks from our home, and during the summers the Handlers and the Stettens have seen a great deal of each other. Phil and Lucy have two sons and currently two grandchildren. It is perhaps the absence of a daughter in the Handler family that

directed Phil's attention to my own flock. A process of mutual adoption has occurred between my daughters and the Handlers. Lucy has recently reminded me of an episode which occurred after an all-night session of the coauthors of our textbook. It was at my home that our conference was interrupted by sunrise and the awakening of my three daughters. The two elder girls came into the room and commented on our unshaven and disheveled appearance. When Mary, my youngest daughter, arrived on the scene, she promptly sat on my lap, stroked my chin, and said, "Nice fuzzy Daddy!"

Philip grew up in metropolitan New York City. He was always an omnivorous and retentive reader and has told me that as a small boy his mother would take him each week to the library where he would sign out seven books, the maximum allowed. He graduated at a very early age from the College of the City of New York, which has been a remarkable training ground for men of learning. He did his Ph.D. work at the University of Illinois under Herbert Carter with whom he has preserved a close relationship. He soon moved to the then young Duke Medical School where he progressed rapidly to the endowed James Biddle Duke Professorship of Biochemistry and chairmanship of the department. Then, in 1969, he was elected to the presidency of the National Academy of Sciences. Lucy and Phil moved to Washington and took up residence in their official home in the Watergate Apartments. He served in that office until the conclusion of his second term in June 1981. During my service on the Council of the National Academy of Sciences, I had ample opportunity to watch Phil as he led that slow-moving and somewhat stodgy society into new pastures. After our return to Bethesda in 1970, we often saw the Handlers in Washington as well as in Woods Hole. Whenever in the course of our careers either Phil or I encountered frustrations and problems, it was our habit to commune with each other. I know I derived much benefit from these contacts and I believe that Phil also was fortified by my support.

Over the years Lucy's disease has progressed with occasional remissions. She has now lost the use of her legs and is more or less permanently committed to a wheelchair. Her hands and arms fortunately are minimally affected. Her wit, if anything, sharpened, her courage in the face of adversity has been indomitable, and she provided Phil with much social and domestic support. During the summer of 1981, Phil's health rapidly deteriorated and he died in December of complication of a hiatiocytic lymphoma.

Phil was always an outspoken, innovative, and courageous leader. He served his major professional society, the American Society of Biological Chemists, in several roles, finally as president. He served similarly on the National Science Board, which is the governing board of the National Science Foundation, and he performed many valuable services to the National Institutes of Health. He weathered personal attacks from Congressman Fountain and newsman Daniel Greenberg, among others. He was, unfortunately, too thin-skinned to sit entirely comfortably in the role of a successful politician. It was during his presidency of the National Academy of Sciences that a determination was made to celebrate the hundredth anniversary of Albert Einstein' a birth by commissioning a large statue of Einstein by Robert Berks, to be situated on the grounds of the NAS facing Constitution Avenue. Despite the fact that the statue elicited a wave of criticism, Phil stuck to his guns and today it is quite generally agreed that the monument is one of the more attractive features of the Mall in Washington, D.C. It is particularly gratifying to see children being photographed while climbing up and about the monument as if trying to assimilate greatness by contact with that gentle genius.

Despite his many years of separation from the research laboratory, Phil continued to be a scholar of biochemistry. He persisted in the re-editing of our textbook through several editions in spite of his many other burdensome obligations. He was of great value to American diplomacy, functioning both as a representative of the State Department and of American science in many foreign negotiations. Together with Lucy, he brought to the Academy a new high level of cultural activity marked by exhibits of art, concerts, and lectures on diverse topics.

Chapter XI

ON THE BANKS -- THE GOOD

On the banks of the old Raritan,
Where old Rutgers evermore shall stand,
For has she not stood,
Since the time of the flood,
On the banks of the old Raritan.

Nine of the colleges founded in this country in the years before the American Revolution have survived. One of these, Columbia, was founded as King's College. It acquired Manhattan real estate tracts, one of which subsequently became Radio City, and it has prospered. Another, Queen's College, sponsored by the Dutch Reformed Church, also acquired real estate but this turned out to be predominantly farmland in the state of New Jersey. It subsequently assumed the name of Rutgers College, to honor a relatively minor benefactor who was a captain in the Revolutionary Army. Under the Horrill Act, Rutgers became the land grant college of the state of New Jersey in 1864, and in the 1940s it became the State University of New Jersey. In the opening years of the nineteenth century, a small college called Rutgers Medical College was established in Manhattan by dissident faculty members of the College of Physicians and Surgeons and, to meet statutory requirements, was affiliated with Rutgers College. This school, however, survived for only a few years.

New Jersey was slow to establish a medical school of its own. Its great private university, Princeton, has always been unwilling to enter the field of medical education, probably guided chiefly by economic motives. In the 1950s, there was a strong movement to establish a medical school in connection with Rutgers University. Rutgers was, after all, the State University and New Jersey was one of the most populous, one of the most heavily industrialized, and one of the most affluent states of the Union. It was also one of the most parsimonious. Its sons and daughters had found that they had to leave the state in exceptionally large numbers in order to secure their higher education and their professional training. Other states resented this and often made it difficult for New Jersey residents to be admitted to their publicly supported universities and medical schools. These matters came to a climax in the early

1950s when it was determined to go to the electorate with the proposal of a large bond issue designed to permit the construction of a medical school. What was not generally recognized at that time was that Seton Hall, the university of the Roman Catholic Diocese of Newark, was planning to establish a medical school of its own. The Seton Hall College of Medicine and Dentistry was located in Jersey City, with a population of approximately 295,000. Legal ownership was vested in the Seton Hall College of Medicine and Dentistry, which was incorporated August 6, 1954. It was associated with the Jersey City Medical Center. The first class of candidates for the M.D. degree was admitted in September 1956 and graduated in 1960. The authorities at Seton Hall and in the Catholic hierarchy apparently saw the possibility of a state-supported medical school as a threat to their plans, and they therefore mobilized to defeat the bond issue referendum. The battle was waged with considerable heat, terminating on the Sunday before Election Day with a pastoral letter that was read from the pulpit in every Catholic church in New Jersey. The tenor of this letter was to instruct all the faithful to vote "nay" on the bond issue referendum. This action was apparently successful and the bond issue was defeated in 1954. The accompanying flyer is a sample of the kind of propaganda which was distributed by the Catholic Church at this time.

The matter lay idle for several years until about 1960 when the board of governors of Rutgers University, under the leadership of its president, Mason Gross, determined that the time had come when Rutgers must mature into a full-fledged university. By this time Rutgers already had faculties of law, agriculture, and engineering, a college for men and a college for women, a graduate school, and campuses both at New Brunswick and at Newark. A survey of other state universities revealed that most of them also had medical schools. Because of the earlier experience it was decided this time to proceed with the founding of a medical school without a state bond issue. At that time, the Association of American Medical Colleges, supported by the findings of the so-called Bane report of 1959, dictated that more medical schools and more medical students were needed to meet growing physician demands. A substantial grant was obtained from the W. K. Kellogg Foundation to provide initial funding for the medical school. A search committee, chaired by Professor James Allison, with Professor David Denker serving as the president's deputy, was established and candidates for the job of dean were reviewed. It was in this context that I was first approached in 1961.

Probably everyone who has gone through medical school has, at some time or other, considered how he would run a medical school if given the opportunity. I had some rather positive notions that I wished to put to the test, and I was therefore interested in the overtures from Rutgers. However, when I visited New Brunswick, I learned to my dismay that what the committee had in mind was far less than I had anticipated. It was their notion that a two-year medical school could be constructed by making a few additions to an already existing Department of Biology. They felt that subjects such as anatomy, biochemistry, physiology, and microbiology could be taught by faculty already on hand. All that was needed was to add departments of pathology and pharmacology to complete a two-year basic medical sciences school as an excrescence on their Biology Department. This plan was what might have been expected from a committee on which there was no physician and, in my opinion, left a great deal to be desired. The resultant school would be doomed in perpetuity to be a second-class operation. I therefore returned to Bethesda with my enthusiasm dampened. As I learned subsequently, the committee explored its proposal with several other candidate deans and received negative responses from all. The members therefore concluded that perhaps they were wrong. They accepted the critical opinions that I had sent to them, which must have been shared by other candidates. When they invited me back to New Brunswick in 1962, the proposal was entirely different. It was now agreed that a free-standing, two-year medical school with its own faculty accountable to its own dean was a reasonable first step. It was clear to me from the beginning that two-year schools, if they are any good, do not stay two-year schools, but grow to become four-year schools as soon as they can establish their clinical teaching facilities. I had long discussions with members of the committee, particularly with David Denker and Joseph Lampen, then director of the Institute of Microbiology. I remember the advice of Bill McElroy at Johns Hopkins, which was to consult with the two Senators from New Jersey about the attitude of the state. I had a pleasant but not helpful meeting with Senator Case and a brief and unproductive encounter with Senator Williams.

I discussed the prospect of becoming a medical school dean with a number of acquaintances. Among these, Stanhope Bayne-Jones had been the first chairman of microbiology at the Medical School of the University of Rochester. He subsequently became dean at Yale Medical School, a position from which he retired about 1940. He served as director of the New York Hospital and filled many

distinguished consulting positions. He finally settled in the Washington area close to his beloved Cosmos Club. When I called upon him, he was in an office of the Medical Corps of the United States Army where he was superintending the completion of a history of this service. I told him of my plans, and a far-away look came to his eyes. "Dean," he said, "I was once a dean. That was many years ago. It was a tough job and my faculty soon came to dislike my memoranda; in fact, I learned that they referred to me in the corridors as the czar. I did not like this and so I took to signing my memoranda Bayne-Jones, Czar-Dean. And I'll tell you what a czar-dean is. It is a poor fish who has lost his head, who is generally well oiled, and who ends by being canned."

I also met with the Rutgers president, Mason Welch Gross, on several occasions. I recall that as our conversations approached a successful conclusion, I told him that there were two expectations which I hoped to see fulfilled during my future years at Rutgers. In the first place, I wished to see my medical school building decorated with blowups of the "Muscle Men" from Vesalius' book De Humani Corporis Fabrica. This expectation was gloriously fulfilled and the great hall of Rutgers Medical School now is decorated with excellent photomural reproductions of these famous woodcuts. In the second place, I hoped on some occasion to participate in an academic procession for which the Rutgers band, possibly supported by the Rutgers glee club, would perform the "March of the Peers" from Iolanthe:

Bow, bow, ye lower middle classes!
 Bow, bow, ye tradesmen, bow ye masses!
 Blow the trumpets, bang the brasses!
 Tan-tan-ta-ra! Tzing, boom!

This latter expectation has never been fulfilled.

Mason Gross was a great man by any standard. He had served Rutgers as professor of philosophy, as provost, and now as president. His personality dominated both the faculty and the board of governors. His intellectual interests were both wide and deep. He was extremely well read, being a judge of the National Book Awards, and he had fine taste in art as well as in music. He was a better than average performer on the piano, and supported by his friend Julius Bloom, then director of Carnegie Hall in New York, he provided to Rutgers an exceptionally fine series of musical events. He was, in addition, a man of enormous charm, great wit, and a temper quick to be aroused and quick to

subside. It was while serving under Mason Gross that I became impressed with my personal requirement for job satisfaction-- that my immediate superior be someone whom I could thoroughly respect.

As the senior physician on the Rutgers University campus, I took it upon myself to give medical advice to Mason Gross. He was a heavy cigarette smoker, and I advised him--as the Surgeon General had advised the people of the United States--that smoking was bad for his health. He smiled urbanely and said that he had already decided how he was going to die. I naturally inquired into his plans and he told me, "I shall die by being run over, and I intend to be run over by a Rolls Royce." In fact, shortly after my departure from New Brunswick, Mason Gross was found to have a cancer of the large intestine. This was treated surgically but soon thereafter he developed carcinoma of the esophagus, which ultimately proved fatal.

Mason was initially profoundly ignorant of the affairs of medical schools. He had never visited one, and one of my first functions was to commence his education. He was a fast learner and soon came to appreciate the costliness to a university of the operation of a proper medical school. From the very start, it was my intention to create in New Brunswick an absolutely first-class institution. This was an unfamiliar notion in New Jersey where excellence, particularly in public educational institutions, was not appreciated. It was, I believe, my insistence upon quality which first established a good relationship between Mason Gross and myself.

Whereas I was never able to entice Mason to visit a medical school, I did persuade the provost, Richard Schlatter, to accompany me on a visit to the relatively young medical school at the University of Washington in Seattle. I believe this was for him an eye- and mind-opening experience. He first learned of the size of the needed physical plant, the size and cost of the faculty, and the high faculty-to-student ratio which is characteristic of good medical schools. All these matters were carefully explained to us by Dean George Aagaard and Associate Dean John Hogness.

One of the citizens of New Brunswick to whom I was introduced very early was Robert Wood Johnson, former chairman of the board of Johnson & Johnson a man who had devoted his life to public service and building a family-owned business into a major international corporation. Johnson & Johnson was even then completing the construction of an imposing high-rise Georgian office building directly across the street from the main campus of Rutgers University. New

Brunswick was the home office of the far-flung industrial empire which had been founded alongside the Raritan River three generations earlier. The General, as he was widely known, had served the Federal administration during World War II in some business or supply function. He was considerably my senior, a dignified and exquisitely courteous gentleman who had definite opinions on most topics. His personal wealth was estimated to be approximately \$1 billion. He was an enthusiastic "off soundings" yachtsman and an aviator. I met him on a number of occasions, generally in his New Brunswick office and sometimes in a J & J guesthouse which, like our own home, fronted on the Delaware-Raritan Canal. On one memorable occasion Marney and I were invited to his Princeton home for dinner. As it turned out, we were entertained by Mrs. Johnson, the General at that time being delayed in transit across the North Atlantic from Scotland in his newly constructed yacht.

General Johnson took an immediate interest in the prospect of a new medical school in his town of New Brunswick. He was full of advice on such matters as choice of architect, relations with the local medical community, affiliation with local hospitals, and the need for the construction of bomb shelters to house faculty and students when the next war came. Early on he pointed out to me the desirability of publishing a newsletter revealing the course of development and growth of the medical school and generously offered to fund this activity. As I recall it, the bill each month from the printer was \$300 or less. These bills I faithfully forwarded to the General's secretary and they were promptly paid. After about one year I received a peremptory note from the General indicating that we were now big boys and should stand on our own feet. Further funding of our newsletter by General Johnson was abruptly discontinued.

Robert Johnson was thoroughly familiar with the curious political forces that operate in the state of New Jersey. He had been a candidate for the governorship at one time or another in both of the major political parties, but had never been elected. He was on intimate terms with all recent governors and most of the high officials of the state. For these reasons he was a valued friend of our school. It was his opinion that the school would never be able to have a teaching hospital of its own. If this were an essential component, he suggested that I might as well quit. He observed an armed neutrality with Mason Gross, with whom he disagreed about almost everything. Mason Gross was politically very liberal. Robert Johnson was, I was told, a principal

supporter of the John Birch Society, an arch conservative group. I avoided all discussion of political issues during my meetings with the General.

Probably symbolically, the General had built into his splendid new office building an oval office for his personal use. This was an imposingly large room on the top floor with windows overlooking the principal dominion of his empire. From here he could inspect the parking lot of J & J, in which the cars were all placed very neatly in rows, and across the street the parking lot of Rutgers University, with the cars in helter skelter locations. He pointed out this contrast to me on more than one occasion, muttering something like "I can't think what Mason has in his mind." One feature about General Johnson which I must stress is that he, as did Mason Gross, responded sympathetically to the notion that if there were to be a medical school at Rutgers it had to be the best one that we could possibly build. He was one of the few voices in the state of New Jersey that spoke out loud for quality. Although he personally was a pillar of financial support to both St. Peter's and Middlesex Hospitals in New Brunswick, when his own turn came to need hospitalization he entered the Roosevelt Hospital in the city of New York. It was characteristic of citizens of New Jersey that when they needed specialized education, specialized medical care, opera, ballet, theatre, and many other services, they abandoned their home state for the more fertile areas of Philadelphia to the south and New York to the north. New Jersey was regarded as a corridor connecting these two cities.

As dean of a new medical school, I obviously had much to learn. My activities over the ensuing years included such unfamiliar matters as fund raising, drafting of legislation, addressing medical and fraternal organizations, soliciting support from men of politics and men of wealth, and selecting and treating with architects and engineers, as well as more familiar activities such as recruiting of faculty and establishing educational and research programs to be housed in our new school. In certain of these activities I derived much help from David Denker. David had played a major role in the planning of some of the major new undertakings of the State University, and in generating support from foundations, individuals, and corporations. When David left Rutgers in 1967 to take the presidency of New York Medical College, Dr. Gross said: "The most important of these undertakings is the new Rutgers Medical School, where his efforts in getting non-state support made it possible to start the development of a school which is now a reality. For this

achievement in particular the people of New Jersey are greatly in his debt." David, formerly a newspaperman, had earned a Ph.D. in history at Yale and had been a member of the Rutgers history faculty, but by the time that I arrived he was a special assistant to the president of the university. He was told to give me guidance, particularly in the area of fund raising, something with which I had had no experience whatsoever. New Jersey abounds in pharmaceutical manufacturing corporations and these were an obvious target for our activities. We called upon the presidents and other high officials of most of these companies in the course of the next few years and were, in general, given a hospitable reception. The typical corporate gift to a new medical school seemed to be between \$50,000 and \$100,000. David and I finally collected from private and corporate donors in the neighborhood of \$4 million.

One of our largest gifts came from Merck, where my friend Max Tishler was now a vice president. The reason for the size of the gift is curious. Apparently the board at Merck had voted to give the usual \$100,000 to the new Rutgers Medical School. However, an untoward event occurred. Sometime earlier a raid on the Bay of Pigs on the Cuban coast took place, manned, it was generally believed, under the direction of the CIA. The Cubans took many prisoners whom Castro held as hostages against the delivery of certain commodities, particularly medicines, of which he stood in need. The firm of Merck at this time made what appeared to be a singularly generous offer. It gave to Cuba medicines valued at \$1 million, and sometime thereafter the hostages were restored to the United States. A Washington newspaper columnist, exploring the terms of this gift, had discovered that in effect the gift was self-serving. The tax law provided that the full market value of the manufactured product could be deducted from income in the event of such a contribution. Since the firm of Merck was then being taxed at a rate of about 50 percent, the gift effected a tax saving of approximately \$500,000. Whereas the sales price of the manufactured articles came to \$1 million, the actual cost of manufacture was one-fourth this figure, or about \$250,000. Thus, in making a gift of \$1 million worth of manufactured drugs, Merck in effect saved \$500,000 in taxes at a real cost to them of \$250,000. This newspaper expose of the real nature of their purported gift was embarrassing to members of the Merck board, and they directed their president, Mr. John Connor, to divest himself of a quarter of a million dollars. This figure was added onto our \$100,000 gift and therefore the check which he turned over to Mason Gross and me was in the amount of

\$350,000. I recall that on the ride back from Rahway to New Brunswick I suggested to Mason that we rename the medical school after its largest single financial benefactor, Castro.

Another significant contribution to our fund was made by the Commonwealth Foundation. When David and I explored the interests of the Commonwealth Fund, it turned out that the establishment of our library of medicine appealed to them. It was soon agreed that they would make a contribution of \$450,000 to the book collection. They did express concern that such a gift might be offset by corresponding reduction in the size of the state's appropriation for the same purpose. Their gift, under these circumstances, would simply have the effect of saving money for the taxpayers of New Jersey. We therefore produced our big gun, Mason Gross, and he assured them that under no circumstance would such a cut in state appropriations be tolerated. The gift was made and we were soon in the business of building a fine Library of Science and Medicine close to the Medical School, of hiring Mr. James Barry of the staff of the National Library of Medicine, and of collecting the many sets of journals which would be needed by future generations of our faculty and students. Subsequently, of course, the inevitable happened. When the parsimonious New Jersey Legislature discovered the magnitude of the gift made by the Commonwealth Foundation, they promptly cut their modest library appropriation.

In the course of all these activities I was invited to give talks to many and various audiences. I addressed chambers of commerce and ladies aid societies. I spoke at lunches of the Lion's Club and learned the function of the Tail Twister. I tried to explain to much of the citizenry of New Jersey the many advantages that would accrue to them when, and if, an excellent medical school was established in their state. Most of these talks were well received. Many New Jersey residents were interested in upgrading the quality of medical care available to them locally and in having state-supported medical education for their children. Only when I spoke before meetings of the county and state medical societies did I sense both hostility and anxiety generated by the prospect of an academic medical center in New Jersey. This was a manifestation of the well-recognized "town versus gown" confrontation which has been encountered with the birth of virtually every new medical school.

The site of the medical school had been selected before my arrival. The university had outgrown its real estate holdings within the town of New Brunswick and had spilled over to the other side of the Raritan River, to the

township of Piscataway. All of the newer science buildings had been concentrated at this point, including a large biology building, a chemistry building, a School of Engineering, a recently completed physics complex, and the Institute of Microbiology, which had been established with funds earned as a result of the discovery of streptomycin by Selman Waksman, a Rutgers professor in the School of Agriculture. The patents on this discovery had been licensed to the firm of Merck and the income was, in part, paid to the university. It was these funds that provided the support for a large Georgian building. It was in this general area that the Medical School and the Library of Science and Medicine were to be built. There was also a new construction planned for the Department of Mathematics and a new home for the Center of Alcohol Studies which was being moved from Yale University. It was the idea of the librarian of Rutgers University, Donald Cameron, that a separate and discrete branch of the University library, to be called the Library of Science and Medicine, should be housed in the midst of this newly developing science campus, and we all felt this to be an excellent idea. Under the guidance of Jim Barry, the library building was planned and constructed and the book collection was commenced.

Meanwhile, we proceeded with the planning and design of our new medical school. There was considerable guidance available both from the National Institutes of Health, which in those days contributed to the funding of new construction, and from the Association of American Medical Colleges. We were soon contacted by Lester Goraline, who headed a firm devoted to the programming of new construction for medical schools, hospitals, and related health science buildings. I became very much involved in the construction of a program. Clearly, I first had to learn what an architectural program actually was. For the benefit of my uninformed readers, it is in fact a detailed description of all the rooms in the projected building including a consideration of the functions to be performed in each room, the desirable contacts between the occupants of several rooms, and even such details as the nature, size, and number of pieces of furniture and equipment which each room should contain. The general philosophy which I soon absorbed was that a working building such as a medical school is best designed from the inside out. By this I mean that the skin of the building is the last element of design. The several rooms and all the arteries that connect them, which include all of the services as well as the passageways, must first be considered. Of prime importance is that the

building should function properly. How it appears to the outside world may be of deep concern to the architect and to the neighbors but is of less interest to the occupants.

While our program was being completed by Lester Gorsline Associates, we proceeded with the matter of selecting an architectural firm. Here I encountered an interesting phenomenon. Whereas I received no particular counsel or criticism of my selections for the chairmen of the departments while these were being recruited, when it came to selecting an architect everybody wanted to get into the act. This included not only the president and officers of the University, but indeed nearly every member of the board of governors. It would appear that every man fancies himself an authority on architects and architecture and has high confidence in his own opinion. The actual selection of the architect was determined by the assembled board of governors of Rutgers University after each competing architectural firm had made a presentation. To my mind, far and away the most vivid presentation was made by Stanley James Goldstein, representing a young and relatively unknown firm, McDowell-Goldstein. They had recently completed the design of the physics building on the Rutgers Piscataway campus which was truly handsome and very functional. I was able to persuade the members of the board that here were our architects, and I never regretted this decision. Jim Goldstein had never designed a medical building before but he entered our project as a substantially full-time commitment for a matter of the next two or three years. Together we visited a number of recently constructed medical science buildings, and while he studied the architectural features I made him listen to the comments of the occupants, favorable and unfavorable. I well remember our visit to the laboratories of the Johnson Research Foundation at the University of Pennsylvania. This building had been highly regarded as a product of the pen of Louis Kahn, a famous architect and member of the faculty of architecture at the University of Pennsylvania, and had won an architectural award. It was splendidly proportioned on the outside, but a failure in many regards on the inside. It had an irregular pattern of fenestration which placed windows, curiously, in the very location where one had to place secretarial desks. Thus to the delight of passersby, the knees and legs of the secretaries were all clearly on display. The frame of the building was made of prestressed concrete beams which apparently are quite flexible, while the floors were poured out of concrete which is, I gather, quite inflexible. As a result, within a very short time cracks developed in every floor.

The Johnson Foundation building was highly regarded by everybody except the unhappy scientists who were forced to live in it. They found many operational flaws which I was happy to have called to the attention of Jim Goldstein. Although very modern materials had been used, these were not in harmony and cracks developed on each floor in substantially identical location. This was called to my attention by a Japanese physiologist, who kept a kettle of tea on a hot plate at all times. To dramatize his criticism, he picked up the kettle and poured hot tea onto the floor, where it rapidly leaked through the cracks. He commented that this would cause no flood on the floor below, since there were cracks in the very same location at that point. In order to maximize the so-called net-to-gross ratio, there were essentially no corridors. One had to pass through secretarial spaces in order to go from laboratory to laboratory, much to the annoyance of the secretaries. These and many other features of this building were made explicitly clear to Jim Goldstein during our visit and were points that he, as an architect, might well not have noted.

In this fashion we visited new laboratories at Stanford, the University of Southern California, and the University of California at Los Angeles. We also visited the extraordinary Holmdel buildings of the Bell Laboratories. Here for the first time I studied a totally glass-enclosed building with exterior corridors and windowless rooms, a pattern which we incorporated into portions of the Rutgers Medical School building and which has been used in many modern research buildings. The basic plan provides that every laboratory module back onto a service corridor through which pass all the ducts and wires that a laboratory may require. These include the individualized ducts from fume hoods specified by the Atomic Energy Commission. An ingenious system of interconnections devised by Jim Goldstein permits the easy isolation of any one module from any particular service without interruption of that service to other modules. The system depends upon the presence of two distinct risers, and it was my pleasure to point out to Jim that what he had invented was remarkably similar to the Arterial Circle of Willis in mammalian anatomy, depending as it does upon blood supply of two carotid arteries and permitting the secure distribution of arterial blood to all parts of the brain.

The eventual plan for the basic medical science buildings for Rutgers University provided two connected components--a research tower about seven stories high, one floor assigned to each department, and a teaching building made up largely of "multipurpose" laboratories so constructed that all the

basic sciences except gross anatomy could be accommodated at different times in a single room. For a variety of reasons, this plan was felt to be superior to the older scheme of providing a teaching laboratory for each of the basic science departments. The system has worked quite satisfactorily, in part due to the coordination of the uses of the laboratory by a dedicated faculty member, Tom Stevens. The teaching facility is only two stories above ground, obviating the need for students to use the elevator services, a cause of terrible traffic jams in high-rise medical schools. In addition to the usual conference and lecture rooms, it contains a rather dramatic main hall and it was here that Jim Goldstein displayed the greater-than-life-size blowups of the "Muscle Men" of Vesalius, arranged in such sequence as to display the continuity of the backgrounds in these extraordinary 16th century wood engravings. In the original plan we provided for a rather large bookstore area, feeling that this is an essential component of any substantial literate community. It was my hope that this bookstore would serve not only the needs of the medical school, but also those of the other science personnel of Rutgers University. Unfortunately, since my departure, this area has been partly cannibalized by the expanding needs of the administrative staff.

During the years of planning I saw Jim Goldstein almost daily. He consulted with each of the faculty members as they were recruited, and visited many medical school buildings, generally accompanied by one or more members of the faculty. It was clearly for him an exciting and educational experience, and at its conclusion he was something of an expert in the principles of design of medical schools. He subsequently designed the Medical College of Wisconsin in Milwaukee. Of all the architects with whom I have had dealings, whether in New Jersey or in Bethesda, Jim was most remarkable in his willingness to understand the functional needs of the scientists and to incorporate these into his blueprints. Other architects with whom I have worked seem mostly to be concerned with the construction of monuments to themselves. I honestly believe that Jim fully grasped what would happen in his medical school building and provided for our needs remarkably well.

To prepare Jim for his task, I arranged to take him to many other medical school constructions. George Harrell was at that time dean of a new medical school under construction at Hershey, Pennsylvania. He had had prior experience at Duke and at the University of Florida, and was therefore one of the most experienced of medical school deans in the problems of new buildings. We

visited Hershey, only to find him in a state of utter frustration. His plan, as I recall it, involved a separate building for animal care some distance away from his basic science building. These two were to be connected by a subterranean passage, or tunnel, and at the time of our visit the tunnel already existed as a trench connecting the two major excavations. It had yet to be roofed over. A totally unforeseen problem had arisen when the United Mine Workers determined that they had not been consulted and to dig a tunnel in the state of Pennsylvania without their approval was impossible. A general strike was called and all labor was taken off the project. Harrell had repeatedly explained that his tunnel was really only a ditch, that it was in no way connected with the operations of coal mining, and that he really did not see why the United Mine Workers should be concerned. He ultimately had to go to Washington and right to the top of the National Labor Relations Board to secure a release which would permit his construction to proceed. Immediately upon our return to New Brunswick, I instructed Jim Goldstein to delete the word tunnel from our own blueprints wherever it occurred and to substitute some other word, such as connecting link. It turned out, however, that the United Mine Workers were not active in the state of New Jersey and we were therefore not in this particular jeopardy.

When I first moved to New Brunswick, the Department of Biology placed a couple of modules at my disposal. My first recruit was Bill Hillis, a young administrator then employed at the NIH. He became our business manager and at once the size of the Rutgers Medical School staff doubled. Our next recruit was Enid Hirsch, who has served not only as my secretary but also as the secretary to each of the several successive deans since my departure. She has made Rutgers Medical School her business and, indeed, a substantial part of her life. Endowed with a remarkable memory, she has an endless fund of information about the early history of our school.

Meanwhile, I was engaged in the serious business of recruiting departmental chairmen. While I originally favored the notion of having a single basic science department, I soon discovered that the persons whom I wished to attract to the faculty were of quite a different opinion. I therefore agreed to a traditional structure with six basic science chairmen. I did, however, insist that two clinical departments, namely medicine and psychiatry, be represented very early in the assembling of the school. My first recruit was Walter Schlesinger, with whom I had worked fairly closely at the Public Health

Research Institute. He was, at that time, chairman of microbiology at the medical school of the University of St. Louis, a Catholic school which was having serious problems. At the time of his arrival, we had, of course, no laboratory buildings in which to house his activities. Fortunately the Colgate-Palmolive Company had just finished a very handsome research building in the immediate neighborhood. It appeared that with an eye to the future they had constructed more laboratory space than they needed at the moment and they were happy to accommodate Walter Schlesinger and some of his initial associates for a period of time. Walter assembled a group of gifted microbiologists and he administered this department with remarkable success. To the best of my knowledge, not a single member of his faculty has left Rutgers Medical School. At the time of this writing, Walter is in the process of retiring as chairman and the search for his successor is under way.

My second recruit was Albert Silverman, a psychiatrist working at that time at Duke University. He ran me to ground at a meeting of the Association of American Medical Colleges and sold himself to me. I had not met him previously. He was full of many exciting ideas in the area of psychiatric education for basic medical science students, which I found very appealing. He put together a varied but small Department of Psychiatry, and before his departure he had funded and constructed a modest psychiatric clinic, which was in fact the very first clinical facility owned and operated by Rutgers Medical School. Shortly before I resigned, Al was invited to assume the chairmanship of the Department of Psychiatry at the University of Michigan in Ann Arbor, a very important and prestigious post which he accepted.

The remaining basic science chairmanships were filled by Robert Crane, a biochemist whose work on sugar transport I had long followed, who came to Rutgers as chairman of physiology; Bruce Breckenridge, who assumed the chairmanship of pharmacology; Gerhart Plaut, who came to us as chairman of biochemistry; and Ashton B. (Archie) Morrison, formerly on the faculties of Duke, Pennsylvania, and Rochester Universities, as chairman of pathology. The appointment of Arthur Hess as chairman of anatomy completed the basic science roster.

The Department of Medicine presented problems. I wished to bring to the campus a scientifically oriented physician, but I could not provide him with the needed clinical facilities. As yet we had no hospital nor any prospects of building one. The community hospitals in New Brunswick, while interested in

our activities, were very coy when overtures were made to them to become university teaching hospitals. I had recruited, contrary to my habit, a junior faculty member into the Department of Medicine, in the absence of a designated chairman. This was LeRoy Pesch, whom I had known as a research associate at NIH. He was a product of Washington University, St. Louis, and after serving his time in Bethesda under the guidance of my friend Yale Topper, he had accepted a position at Yale Medical School. Here, it turned out, he was quite unhappy and therefore was very willing to move to Rutgers with his delightful wife, Barbara, who was trained in botany and in landscape gardening. As I surveyed the field of possible candidates for the chairmanship of the all-important Department of Medicine, I was advised that Roy Pesch was himself an excellent candidate. After careful deliberation, the matter was discussed with him and he became, I believe, the youngest chairman of a department of medicine in the United States. This appointment proved to be a mistake. Roy did not have the stature to assemble an appropriate department and he was not able to establish harmonious relations with the private practitioners of medicine who abounded in the New Brunswick area. Without my knowledge he negotiated with his former preceptor, Robert Glaser, who had earlier extolled Pesch's virtues, and one day Roy announced to me that he was leaving to become dean of Stanford Medical School. It subsequently developed that in actual fact he was to become an associate dean. He packed the equipment which had been purchased by Rutgers Medical School against a grant for which he was the principal investigator and unceremoniously departed. His subsequent career consisted of short stays as dean of the State University of New York's Medical School in Buffalo and as president of Michael Reese Hospital in Chicago. His career at Michael Reese ran into difficulties and I am not certain what his present activities are. All in all Roy Pesch was the only serious disappointment that I encountered in the process of assembling the senior faculty at Rutgers. As a younger man he was very attractive and my own feelings toward him were approximately paternal. I had fully expected to watch his career as a scientist and physician flower and hoped to have a hand in this process. A number of years ago I was invited to the Michael Reese Hospital to talk at a symposium on amniocentesis. Roy, then its president, took me out to breakfast and we tried to maintain a conversation, but we both found that we had little to say to each other.

I had a far more happy association over the years with another member of the Rutgers faculty-namely, Richard Cross. I have known Dick since Columbia days.

While I was at the Public Health Research Institute he joined me as a full-time research associate, devoting his attention to some of the analytical details, particularly in relation to the then novel techniques for the counting of radioactive carbon samples. Dick is a man of imposing physical proportions--very forthright and extraordinarily honest. Whereas he worked faithfully in the laboratory at PHRI, it was clear that this was not his kettle of fish. He was scholarly, studious, and of gentle disposition, deeply concerned with the suffering of humanity, and determined to do something about it. He finally left New York and when I located him next he was associate dean for student affairs at the University of Pittsburgh Medical School. Accompanied by his vivacious Peggy and their five children, he moved to New Jersey to assume, at my invitation, the position of associate dean. He soon expanded his activities to include the founding of a Department of Community Medicine, a department which I had not originally visualized in our two-year medical school but which he made into a very strong feature of student life. The courses he offered included instruction in such matters as drugs, alcohol, sex, and emergency medical care. The lectures that he and his colleagues presented to medical students were understandably enormously popular. I recall that on one occasion he surreptitiously staged for the students a sham automobile accident in the midst of one of his teaching exercises. An old wreck of a car, procured for the purpose, was deliberately smashed very near to our temporary teaching facility. The victims, liberally seasoned with catsup, were found in the car and on the adjoining street when the alarm was sounded. The medical students came trooping out of the school building to react to this terrifying situation. Meanwhile, our art and photography expert, Mr. Ng, had taken a position on the roof of the building and photographed the proceedings with his movie camera. This record then served as a basis for a subsequent teaching exercise in which each student could see how he had actually performed in a crisis situation. Dick was for me a pillar of strength. There were, of course, episodes in which the faculty members disagreed with each other and also occasions when they disagreed with me. I always knew that in these crises I could count on Dick's intelligent judgment. He is a descendant of Thomas Jefferson and I like to think that his wisdom was perhaps derived in part from this genetic stock.

One of the joys of working on a university campus is the access which is provided to scholars in many different fields. I made it a habit to have my lunch at the Faculty Club and there I could sit down with the President, the

Provost, or the Librarian of the University as I chose. In luncheon table conversation with colleagues from many other departments, I learned of the vagaries of running a university press, the problems of the teaching of Romance languages, and many fascinating details of the History of the Byzantine Empire. Such diversity in topics of conversation stands in contrast to luncheon conversation at the NIH, which deals largely with the subject matter and the personalities in biomedical research.

The funding of our medical school construction derived from various sources. Reference has already been made to the contributions from private sources, chiefly the pharmaceutical industry. Approximately \$4 million was collected from these sources. The largest single public contributor was the Department of Health, Education, and Welfare, which acted favorably upon my very carefully composed application for construction funds. These came from two offices. The funding of the teaching spaces was charged to the Division of Hospital and Medical Facilities under the authority of the Hill-Burton Act. The remainder, which was to pay for research spaces, came from the Office of Health Research Facilities and Resources of the NIH, which at that time had substantial amounts of money appropriated for that purpose. The two pieces together came to about \$8 million. A third portion of \$6 million was secured from the state of New Jersey as a result of meetings between Mason Gross and Governor Hughes, who was quite sympathetic to the new medical school. The construction bids came in satisfactorily under budget, and construction commenced in November of 1966. It was supervised on a daily basis, not only by Jim Goldstein and me but also by an officer of the university endowed with the ancient British title of clerk of the works, a title which was borne by Geoffrey Chaucer in the 14th century during construction of the wonderful roof of Westminster Hall in London. Because it was a complex building, construction consumed more than two years.

It was my intention to erect a teaching hospital immediately adjacent to the basic science buildings, with floor-by-floor connections so as to provide every opportunity for intimate association between clinical scientists and basic laboratory scientists. To provide plans for this highly specialized structure, the firm of Skidmore Owings & Merrill was retained and soon developed very elegant plans indeed. An automated materiel distribution system was installed in the sub-basement. Standardized patient bedrooms were designed, each equipped with a bathroom of monolithic fiberglass construction, all of the

appurtances being included in a single molded piece. Some of the associations between clinical and basic activities were self-evident. Thus, surgical pathology in the hospital was on the same floor as academic pathology in the basic science building. Infectious diseases in the hospital was housed on the same floor as microbiology, and so forth. We were very pleased with the building, and had the state abided by its original commitment to provide \$40 million toward its construction, we could at that time have had a good deal of what we wanted. Unfortunately, the state of New Jersey reversed itself and withdrew its support and our beautiful hospital died as a set of blueprints.

Meanwhile we had secured title to a very small one-story laboratory building that had been part of the psychology laboratory of Rutgers University. We added a wing which contained a pair of model 16-man multipurpose teaching laboratories and here we admitted our first class of 16 students in 1966. In order to bar the notion that this might be our final medical school building, I carefully labeled it "Rutgers Medical School Annex."

By this time the Department of Medicine was chaired by Clifford Gurney, recruited from the University of Chicago, a gifted man and a wonderful teacher. He and I gave a great deal of thought to the opening exercises of our new educational venture. We decided that since this was a medical school, it would be well to initiate the students at once into the problems of medicine and to introduce the students to the object of medicine--namely, the patient. On the very first day of the first year of our medical school, the students assembled in one of the teaching laboratory rooms and there they were introduced to a man of about 40 years who suffered from sickle cell anemia, homozygous SS disease. This man was well known in the hospitals of New Brunswick and had, in fact, been kept alive by very many blood transfusions. He was employed as a porter in one of the local hospitals. Cliff Gurney made an elegant presentation of the nature of sickle cell disease. He reviewed its genetics; he reviewed the peculiar cytology of its erythrocytes; he discussed the nature of heme metabolism and the several bile pigments; he even touched upon the apparent intolerance of the plasmodium of malaria toward sickle hemoglobin. The patient thus provided an excellent opportunity to present to the students an indication of the reasons for the study of the several basic sciences: biochemistry, anatomy, genetics, parasitology, etc. Finally it became necessary to present to the students the appropriate diagnostic test. Although the patient had been followed for many years in the hospitals of New Brunswick, there was no

electrophoretic scan of his hemoglobin included in his record. We therefore ran this test, and in order to make the presentation clearer to the students, Cliff had secured authentic samples of hemoglobin A and hemoglobin 3 from friends in New York and had prepared parallel paper strips. He showed to the students the electrophoretic distribution of hemoglobin A with the spot near one end of the paper and of hemoglobin S with the spot somewhat removed. He then showed the electrophoretic pattern that we had just developed on the blood of our patient. Here there was a strong spot at the location of hemoglobin S, but in addition a faint spot clearly visible in the location of hemoglobin A. This was unanticipated and puzzling to the students since they had just been informed that this patient had no genetic information to encode for hemoglobin A. Presented with this puzzle, one of the students, a young woman, immediately saw the resolution of this difficulty and her hand shot up. When called upon to speak, this first day medical student, who might never previously have heard of hemoglobin or of electrophoresis, made an unexpected statement, "You can't fool me. That spot for hemoglobin A comes from the transfusion which the patient received last week." The overwhelming probability was that she was absolutely correct. The experience was very exciting for me and other members of the faculty because it revealed that even from the very beginning, if the proper problem is presented in the proper way, an intelligent medical student can often see the proper solution.

Thus fortified, we felt that we had taken a step in the right direction and, on a weekly basis, we continued clinics for the students throughout their first and second years, the subject matter of each clinic being selected with reference to what the students were learning at that time in their basic science courses. In this way, our first-year students were taken to an institution for the mentally retarded and given a clinic on Down's syndrome, after which blood was drawn from the patients and taken back to the school for karyotype studies. Patients with renal disease were presented concurrently with the instruction of kidney function in the physiology course, and the patients were shown congestive heart failure while they were studying the normal circulation. I have long believed that the patient is the prime mnemonic for the medical student and is not given sufficient prominence during those early years in medical school when the burden on memory is so very heavy. I suspect that none of our 16 students in that first class will ever forget the drama of sickle cell anemia.

It was during these early years that there was considerable political agitation among the students on Rutgers and other university campuses throughout the country. The Vietnam war was in progress. On the main campus of Rutgers University the students were, at least occasionally, deeply aroused. This arousal was further stimulated when a member of the history faculty, at a public gathering, stated that he hoped that the North Vietnamese would win. This statement, which was made outside of the classroom, brought a howl of protest from legislators and alumni and calls for his ouster. I am proud and happy that Mason Gross withstood this wave and insisted that every member of his faculty enjoyed the privileges of free speech and that Dr. Eugene Genovese would, under no circumstances, be separated. An active campaign, which led to the slogan "Rid Rutgers of Reds," was started on a statewide basis, but ultimately died out due to the calm governance by Gross. On the medical school campus there was virtually no political activism and almost no problems between faculty and students. On one occasion, the students did object to a faculty action-- failure to promote one of the instructors in anatomy whose research record was undistinguished. However, I am happy to say they listened to reason when I met with them. I believe that I had the respect and affection of the student body. The class was sufficiently small that I knew them all on a first name basis. I was familiar not only with their academic achievements, but also with many of their marital and financial problems. At a time when students on other campuses were invading the administrative offices and sometimes manhandling members of the faculty and of the administration, my students were overtly affectionate. This they demonstrated in a very personal way when the entire student body, on Christmas Eve one year, came to our home on the banks of the Delaware-Raritan Canal to serenade my family and me with Christmas carols.

When the student body published its first yearbook in 1969, called "Annex," they included the following dedication statement:

It is not at every medical school that a student can meander up the hall, literally bump into the dean and become engrossed in a conversation on any one of a myriad of topics. We are extremely fortunate at Rutgers to have such an environment and the man behind it - Dr. Dewitt Stetten.

We could enumerate the dean's impressive background, honors and publications. We could extol his skills as an administrator, an organizer, a planner, a dreamer and, in these complicated times, a

politician. But, to the student, these qualities are of only tangential importance.

To us, the essence of Rutgers is the friendliness, intimacy and cooperation displayed by faculty and students alike. It is these values which make the Rutgers Medical School experience one which extends beyond the laboratory and the textbook. It is these same values which Dean Stetten has been able to instill, propagate and guide. This was possible largely through self-example--giving seminars, popping in on student presentations, inquiring how things are going, and leaving the door open to applause and complaint alike.

It is with a heartfelt sense of gratitude and thanks for our two years at Rutgers and with consummate faith in the future success of the entire Rutgers Medical Center complex, that we proudly dedicate this, our first yearbook, to Dr. Dewitt Stetten.

This statement was abundant compensation for all of the problems and the headaches that I had encountered in getting the school off the ground. We admitted four classes of sixteen students each between 1966 and 1969 while we remained in constricted quarters. Only when we finally entered our palatial new medical school building in 1970 could the class be enlarged.

As with all medical schools, we had passed through the process of being accredited. Accreditation is performed by a liaison committee to which both the American Medical Association and the Association of American Medical Colleges contribute. We had our visit and we passed the process with flying colors. We insisted that all of our students, at the end of two years, take what was then Part I of the National Board Examination for medical licensure. We were proud to learn that of the more than 100 schools in the United States, we ranked fifth from the top in the average score achieved for that examination. It was clear that, at least by this standard, we were doing a good job. In no small part, the excellence of our achievement was determined by the remarkably high quality of the students whom we admitted. After two years we placed our students into the third-year classes of various prestigious medical schools. During my tenure as dean, one-quarter of our graduates were admitted to the third year of Harvard Medical School.

I continue to see some of these students and can take pride in their achievements. There is Luis Villa, a Cuban refugee, who finished at Harvard Medical School and is now a board certified pathologist and oncologist in Miami. There is Barkley Adams, who left an assistant professorship in physics at Rutgers College to become a medical student in our school and who continued

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his training after Harvard at Presbyterian Hospital in New York. There is Kathy Cooke, who was the first woman to complete a urological residency at the Massachusetts General Hospital and has since become associate professor of urology at Rutgers Medical School. Peter Howley, who spent his spare time in the Department of Microbiology during his Rutgers days, now heads an active research group in the National Cancer Institute. He has become a leading authority on the biology of papilloma viruses.

These are among my happier memories of the days in New Brunswick.

Chapter XII

ON THE BANKS -- THE BAD

In the previous chapter I have told some of the highlights in the process of generating the new medical school in the town of Piscataway on the Raritan. I must now recount some of the problems, the frustrations, and the headaches that we experienced.

A number of new medical schools were in the process of being built at this time in other parts of the country, and almost invariably the established practice of medicine in the community was more or less hostile to the appearance of an academic medical center in the neighborhood. The local practitioners felt threatened by the proximity of a medical school. They were often offended when the new institution failed to provide them with academic titles, and they were unused to the competition in the quality of medical practice that was provided by a nearby university-teaching hospital. All of these matters assumed an exaggerated form in the case of Rutgers Medical School. This was doubtless due to the fact that until very recently there had been no medical school in the state of New Jersey with which the physicians had to contend. They had been free of the quality surveillance which a medical school exerts over the practitioners of medicine in the vicinity, and with few exceptions the local doctors were unenthusiastic--if not openly hostile--to our venture.

Only a few of the local physicians exhibited a genuine and positive interest in what we were proposing to do. Among these I must mention Dr. Norman Reitman, an enthusiastic alumnus of Rutgers College who became Chairman of the Board of Trustees of the University a few years later. Norm was the leading cardiologist in New Brunswick and he became not only a good friend but my personal physician. In addition, he maintained a watchful eye on my mother during the years of her deterioration as a patient in the Parker Memorial Home. He managed to interest a few of his close professional associates in the support of Rutgers Medical School. But this was unusual.

As a part of my routine activities, I accepted many invitations to speak to various groups in the state--county medical societies, hospital staffs, and social and fraternal organizations. In the course of these meetings I made a curious observation. A fundamental part of the business of every competent

medical school faculty is the pursuit of research, which means expansion of the existing body of knowledge. This was an area about which I could wax enthusiastic since it had been my major activity heretofore. I soon learned that the medical audiences that I encountered in New Jersey had a decidedly negative reaction to the word "research." This was a totally foreign and unfamiliar activity to the vast majority of New Jersey physicians, an activity which they were inclined to treat with contempt. Any reference to the biomedical research which might be conducted in this medical school elicited anger and sneers from the established medical practitioners. Curiously, the phrase "medical investigations" was more acceptable, and I therefore schooled myself to try not to use the term "research" but always to call it "investigations." However, these problems were not resolved that easily. The underlying fear, I believe, lay in the prospect of loss of private practice to the professors of clinical sciences who would be imported to join the medical school faculty. Also, the prospect of a first-class teaching hospital to be constructed in central New Jersey was a threat to the often financially insecure community hospitals scattered throughout the various towns and cities of the state. Having made this observation, as may be imagined, I learned to extol the virtues of investigation on the part of my faculty rather than discuss their research plans. I was advised by a number of kindly disposed physicians in New Brunswick that I would gain more acceptance among the local doctors if I joined the Middlesex County Medical Society, and this I proceeded to do, sponsored by my good friend Dr. Norman Reitman. I also rejoined the American Medical Association, a group from which I had separated myself many years earlier. Once I had joined the County Medical Society, I sponsored the membership of several of my faculty members and had therefore to attend the meetings at which they were inducted. At these meetings the topics discussed were entirely political or financial and were singularly devoid of either clinical or scientific interest. The talks of guest speakers had to do exclusively with monetary matters, such as the nature of malpractice insurance, the tax advantages of self-incorporation of the practicing physician, and the many devices available to collect delinquent accounts. Such topics were of more interest to the program committee of the County Society than were recent advances in the understanding, diagnosis, or treatment of disease. Here I was exposed to the more venal aspects of medical practice in the United States, an area from which I had been carefully shielded in my earlier employment. I was dismayed at the

apparent increase in venality of the practitioners of medicine since my own childhood, when I was exposed to the thinking of my surgeon father and his medical and surgical friends who scaled their charges to the patient's resources and treated many entirely free. Mammon had, it appeared, replaced Aesculapius.

One example may suffice to show the kind of reception which the hospitals of central New Jersey gave to new members of the Medical School faculty. The recruitment of our Chairman of Surgery presented peculiar problems. It was obviously not desirable to select a surgeon who would prove peculiarly threatening to the already established practitioners of surgery. We were happy when we found James Mackenzie, who came to us from the University of Missouri as a well-qualified and well-trained cardiac surgeon. It turned out that there was no cardiac surgeon in central New Jersey. He therefore threatened no one. I recall taking him with me to a meeting of the staff of the largest hospital in the neighborhood in the hope of securing operating room and surgical privileges for him in that hospital. Local cardiologists welcomed him, since this would permit surgical treatment of their patients in the neighborhood and would obviate the need for sending their patients to Philadelphia or New York as had previously been the custom. The members of the Anesthesia Department, however, objected strongly. It was pointed out to us that the reimbursement to the anesthetist was much like the payment made to a taxicab--namely, the anesthetist received more for the first 15 minutes of his services than he did for each subsequent quarter hour. It was therefore to his advantage to see many patients requiring anesthesia of short duration rather than a single patient requiring anesthesia for a long period. Since cardiac surgical procedures in general require many hours, the anesthetists foresaw a decline in their hourly income if cardiac procedures replaced the more familiar tonsillectomies which require only a few minutes each. Jim Mackenzie and I were dismayed when his application for surgical privileges was rejected on this basis.

Tonsillectomy was a procedure which had a great vogue among nose and throat surgeons some 40 or 50 years ago. Since that time a considerable body of evidence has accumulated indicating that this procedure does not benefit the patient significantly and may, on occasion, do considerable damage. For this reason the surgeon today is likely to approach tonsillectomy with some caution and to perform the procedure in relatively rare instances. Not so in New

Jersey, which ranked near the top among the states in the incidence of the performance of optional tonsillectomies and hysterectomies. We learned that some of the hospitals dedicated an operating room for one full morning every week to the routine performance of tonsillectomies upon series of small children. The popularity of this procedure was such as to make a surviving pair of tonsils a relative rarity among the adult population. Was this good medical practice or were we observing the result of an overwhelming profit motivation?

As the Medical School and its plans grew and developed, the hostility of the State Medical Society became quite overt. I was invited to address this society at one of its annual meetings, but found myself quite unable to convince the assembled physicians that what we were hoping to accomplish could only be of benefit to them and to their children and would, in no important way, do damage to their present rights and privileges. I had the impression that I made relatively few converts.

It is, of course, true that I came to New Jersey, as did almost all my colleagues on the faculty, out of an academic environment. None of us, as far as I remember, had had any significant exposure to the private practice of medicine. We were repeatedly shocked both by the apparent greed of many of its practitioners and by their startling lack of sophistication in the diagnostic and therapeutic procedures which they sometimes invoked. I well recall the case of my cousin, Roger Ernst, who returned from a tour of foreign duty in the State Department. He did what foreign service officers are prone to do--he was first debriefed and then went to see his dentist, since dentistry in Ethiopia leaves much to be desired. Next he hired a car to drive toward his summer home on Nantucket Island, spending the night at the home of his mother-in-law in New Jersey. Here he became acutely sick with fever, chills, cough, and chest pain. A local practitioner was summoned and he admitted my cousin to one of New Jersey's better known community hospitals. He remained there for about two weeks, still febrile, still undiagnosed, losing weight, and becoming progressively more ill. At the end of this period both his wife, Jean, and the State Department were concerned about his health and suggested that he be transferred to the Massachusetts General Hospital. Jean called me at that time saying that she had heard that the Massachusetts General Hospital was an old run-down dump. I assured her that if I had an undiagnosed serious disease, the MCH was precisely the kind of dump that I would seek out for myself. He therefore was flown up to Boston and a few hours later I was happy

to receive a telephone call from a young physician, Dr. Arnold Weinberg, whom I had known during his term of service at the Clinical Center of the National Institutes of Health. Dr. Weinberg was able to reassure both Roger and me that he had a diagnosis and that Roger would soon be up and well and sailing his boat in Nantucket Sound. In fact, Roger had a pulmonary abscess secondary to aspiration of a fragment of dental filling, an occasional complication of dentistry. It was a textbook case. It responded well and promptly to appropriate therapy. It is frightening to consider what might have happened had Roger not been moved out of the New Jersey environment.

I may add that this assessment of practice in many of the community hospitals of New Jersey was not uniquely my own. I have heard former Governor Robert Meyner say that he was not particularly worried about an accident in which he might become involved on the New Jersey Turnpike, but he was terrified of the hospital to which he would be taken after such an accident. He attributed his father's death to the poor quality of care that he had received in a New Jersey hospital. This evaluation is reconfirmed by the behavior of those who were sufficiently knowledgeable. Governors of New Jersey, captains of industry, and officers of the university, when seriously ill, often moved to the hospitals in New York or Philadelphia. In its medical care, as in many other areas, New Jersey clearly suffers from being situated between two great metropolitan areas. New Jersey exhibits a peculiar parasitism upon New York and Philadelphia for many of its services and its entertainments.

Our major problems, however, did not come from the practitioners of medicine in the state. Rather they arose from a situation that was not of our making. A few years after the establishment of Seton Hall Medical School, its parent university realized that it had made a mistake. The school proved to be an excessive financial burden upon its parent university, which depended for its support upon the Roman Catholic Diocese of Newark. Its president, the Rt. Rev. Monsignor John J. Dougherty, Auxiliary Bishop of Newark, wanted out. The first route to be explored was to try to persuade Rutgers to assume Seton Hall Medical School and operate it as Rutgers Medical School. This proposal was put to me shortly after I moved to New Brunswick. I knew nothing of the financial problems of Seton Hall Medical School at that time, but I had been told by many friends of the very poor quality of this educational venture. There is an agency specifically set up to review and accredit medical schools in the United States. This is the so-called Liaison Committee which

derives membership from the American Medical Association and the Association of American Medical Colleges. The liaison committee, from time to time, sends site visitors to each medical school in the country. The visiting team then drafts a report describing what it has found and specifically listing the defects that it observes in the school under review. These reports, unfortunately, are treated as secret information between the liaison committee and the officers of the medical school in question. They are not made public. However, several friends on the site-visiting team had spoken to me about the extraordinarily poor condition of Seton Hall Medical School as an academic venture. In fact, it was common gossip in medical education circles that Seton Hall was in a poor way. I therefore made a number of inquiries and finally reported to Mason Gross that I personally could not encourage Rutgers University to accept any responsibility for this struggling medical school, that I certainly had not come to New Jersey in the expectation of creating a medical school in Jersey City, a community with a history of political corruption that was scarcely exceeded anywhere in the country. I was pleased to find that Gross had, on the basis of his own explorations, come to exactly the same conclusion. Rutgers University therefore declined the suggestion that it assume any responsibility for Seton Hall Medical School and we proceeded to move full speed ahead on our own. A committee had been established by Governor Hughes to look into the best disposition of what was then New Jersey's only operating school. This committee was chaired by George F. Smith, a distinguished Catholic citizen and a former president of Johnson & Johnson, and had among its members former Governors Alfred E. Driscoll and Robert B. Meyner, John T. Connor, then president of Merck, and Dr. Jerome Kaufman, a cardiologist and president of the Medical Society of New Jersey. There were, in addition, John M. Fasoli, president of the New Jersey Taxpayers Association, Dr. Michael Frost, president of the New Jersey State Dental Society, and Dr. Frederick M. Raubinger, commissioner of education for the state of New Jersey. This committee reviewed the assets of Seton Hall Medical School and ultimately recommended to Governor Hughes that the state of New Jersey purchase Seton Hall Medical School at a cost of approximately \$3 million. In the course of its deliberations, however, the committee listened to the testimony from various witnesses, including myself. I well recall my visit to this committee, sitting in the Essex Club in Newark on a swampy day, June 8, 1964. I was accompanied by my friend and colleague, David Denker, and read a

prepared statement. I was then questioned by each of the committee members. I tried to make my position perfectly clear, that I had been brought to New Jersey in order to establish the best possible medical school in the best possible environment. I personally did not find that metropolitan Jersey City, nor yet the Margaret Haig Memorial Hospital, met these standards. Furthermore, I argued as persuasively as I could for the placement of a medical school--not merely administratively but physically--within the domain of its parent university. I tried in vain to explain to the members of this committee my perception of what an academic medical center must be, and to express my conviction that the state of New Jersey and its state university deserved the very best that could be provided. I reviewed for the members the history of the University of California and its venture into medical education with the initial establishment of a fine medical school in the San Francisco Bay area, followed by subsequent creation of medical schools on its other campuses. I was fully aware at this time that the Liaison Committee had placed the accreditation of Seton Hall Medical School in serious jeopardy. The confidential nature of this information, however, precluded my revealing it to the committee. The members of the committee were distinctly unfriendly toward me, having apparently previously come to a decision as to the best disposition of the medical school in Jersey City. Dr. Denker and I recorded for the president the highlights of the meeting:

The discussion revealed that the commission unanimously rejected the proposal which had earlier been submitted in writing by Rutgers University to the commission. The letter which had been submitted a few days earlier by Dr. Gross had not been reproduced and had not been seen by the members of the commission other than Mr. Smith. . . . The view was also expressed that, whereas in the original flush of the problems at Seton Hall, Rutgers had been callously indifferent, all at once we had become very much concerned only to officiate at the annihilation of Seton Hall Medical School. Governor Meyner did encourage Dr. Stetten to "continue in his dreams" and to "avoid playing politics. It was Dr. Stetten's impression that the commission felt distinctly resentful toward Rutgers University for not pulling the commission's chestnuts out of the fire for them. It was also his impression that the committee had fairly thoroughly come to a decision prior to the present meeting. As the meeting broke up, Mr. Smith asked Dr. Stetten to give careful consideration to any possible conditions under which Rutgers University might be willing to assume continuing responsibility for the operation of Seton Hall Medical School. Dr. Stetten agreed willingly to take the matter under serious consideration.

Feeling that I had not presented my position verbally with sufficient clarity, upon my return to New Brunswick I composed a letter to Mr. Smith, restating and reemphasizing my concerns and recommendations. This letter was carefully studied by Mason Gross, who after several days authorized me to transmit it. (It is David Denker's recollection that George Smith requested of me a confidential letter "for his eyes only." The letter was sent and was seen only by David and President Gross. Any breach of confidentiality thereafter is attributable to George Smith.) The text of the letter, dated June 13, 1964, follows:

Mr. George F. Smith
Johnson & Johnson
New Brunswick, N.J.

Dear Mr. Smith:

After leaving Newark on Monday, June 8, I realized that I had perhaps not made my own position entirely clear. I should like, therefore, to supplement my earlier comments with the following additional facts.

When I accepted the position which I now hold it was with the firm intention to create in New Brunswick a school of the highest quality of which Rutgers University and the State of New Jersey would inevitably be proud. This undertaking, with its many aspects of funding, architecture, philosophy, recruitment, and curriculum, has turned out to be more than a full-time job. My immediate collaborators and I find that there are too few hours in the day to complete the many tasks which must be completed, and too few days in the month to meet the many deadlines which must be met. Neither I nor my collaborators have the time or the energy to assume any additional major responsibilities. We believe that what we are doing is good and is important and we do not wish to dilute our efforts.

For these reasons, it was truly my initial reaction to the newspaper stories about Seton Hall Medical School that this was a problem toward the solution of which we could make very little contribution. Indeed, after discussion with my colleagues, other medical school deans, and Dean McCormack, I am still of the opinion that there is no entirely satisfactory resolution of this long standing quandary in Jersey City. When, however, it was impressed upon me that I must set down on paper the conditions under which I could recommend to Rutgers University that it assume some responsibility for the operation of a medical school in Jersey City or elsewhere, I did give this matter serious thought. You will note that the question, as it was presented, is essentially the same question which you presented to me at the close of Monday's meeting. The position paper dated May 13 which was circulated to you

and which your Commission has rejected was my response to this question.

I am not particularly surprised at the rejection of the proposed solution contained therein. It was, in some degree, devised against my own better judgment. I do not agree, however, with the reason given for the rejection of the proposed solution. The enormous stress which your Commission places upon the continuity of the production of physicians in the State of New Jersey during the next six or eight years is, in my opinion, a shortsighted view. Some discontinuity at this time is a small price to pay for the achievement of high excellence in medical education over the many decades to come. Basically, my objection to the proposal contained in the paper of May 13 is that it is merely an expediency and loses complete sight of the long-term objectives.

In my own analysis of the problem in Jersey City, it is quite clear to me that the real reason why the present sponsors of Seton Hall Medical School are so anxious to divest themselves of their property is not a financial one. Indeed the present sponsors have in effect admitted this if the story which has come to me from two independent sources is true. I am informed that the present sponsors of Seton Hall Medical School have already indicated their willingness to continue the financial support of the school for a period of at least two more years. The real reason why the sponsors wish to divest themselves of Seton Hall Medical School is that it is a focus of both academic and political trouble. The school was conceived in haste and adequate consultation with medical educators was not secured. There were built into the school certain blunders which, after a decade of operation, the present administration of the school has been unable to correct. Among these is a contract with the affiliated hospitals of the Jersey City Medical Center which has proved essentially unworkable. Partly as a consequence of the poorly designed contract, the clinical departments of the school as they now operate are situated in various remote locations tending therefore to defeat the integrated function of the medical school. It is worth noting that despite the best efforts of the dean and his staff these problems have not been resolved. It appears to me entirely improbable that any outside agency stepping into the picture at this late date would have any greater degree of success. I must therefore urge very strongly that the financial responsibility of the future operation of Seton Hall Medical School continue to be vested with its present sponsoring corporation with encouragement from your Commission that the school strive to put its educational program and its clinical affiliations in proper order. When and if such order can be achieved, it may be appropriate for the State to consider assumption of the financial burden of this school. To assume this responsibility at this time with the faculty and programs in a state of chaos would, in my opinion, be a very poor investment of the State's funds.

The above recommendation has not been reached lightheartedly. My colleagues and I have explored various other possible programs wherein Rutgers Medical School might assume responsibility for the

operation of medical schools situated in Jersey City and in New Brunswick. It is, of course, entirely possible to set down various chronologies on paper, including the one recommended by Mr. Connor at the meeting of last Monday, which would provide for a continuous production of physicians in the State of New Jersey. However, before I could recommend any of these plans to Rutgers University I would have to insist that certain standards of educational excellence be met and this, of course, brings us right back to the problems which presently exist in the relationship between Seton Hall Medical School and its affiliated hospitals. To meet the standards which we have adopted for our own use in New Brunswick, it would be necessary for the total professional control of the major affiliated hospitals to be vested with the administration of the school. It would be necessary for the several clinical faculties to be brought back into harmonious operation within the same cluster of buildings. It would be necessary that the chairman of each department and a hard core of faculty be employed by the medical school on a strict full-time basis. It is my understanding that these conditions could probably not be fulfilled within a reasonable period of time.

It would be my hope that, over and above the problem of Seton Hall, your Commission will give attention to the broader and more important problem of total medical education in the State of New Jersey and the State's sponsorship thereof. After a series of misfortunes, including the referendum of 1954, the State of New Jersey has belatedly recognized the propriety of supporting a medical school on the campus of its state university. The design, organization and construction of this medical school is being very carefully thought out. At this very moment, we are completing our architectural preliminaries, and within the next few weeks it is my hope that we shall be applying for the federal matching funds which we expect to secure for the construction of our first building. We are proceeding with due caution in our recruitment and in our plans, and we have never lost sight of our goal which is to generate the very best medical school possible. As you are well aware, it had been the hope of Rutgers University to get this school off the ground without appealing to the State for support. Thus far, in actual fact, the State has scarcely contributed. I would therefore urge upon you and your Commission that you give careful consideration not only to the immediate problem of what to do about Seton Hall Medical School, but also to the question of the prospects for first-rate medical education in the State of New Jersey. I would urge that you secure comparative evaluations of the goals and ideals of the existing medical school in Jersey City and the new medical school in New Brunswick. I suggest that if support is indicated it should be awarded where it will do the most ultimate good. I suggest that a long-range view be preserved, in recognition of the fact that the life expectancy of a medical school, if soundly planned and dedicated to the highest ideals of medical education, is measured in centuries. Alongside of these considerations, the continuity of production of physicians between now and 1970 becomes a small matter.

It is the firm intention of my colleagues and myself to create the kind of a school which we have talked about and which we have dreamed about. I believe that we shall achieve this goal under any circumstances. We can certainly achieve this goal more promptly and with less agony if we have the support of your Commission. I would hope, therefore, that your Commission will consider what we are doing and what we propose to do and perhaps step a little beyond the assigned limits of your function. Certainly an indication from your Commission that Rutgers Medical School is worthy of substantial support by the State of New Jersey would be extraordinarily helpful to us at this stage of our history.

It is documented that the State of New Jersey should, at this time, accommodate not merely two but three medical schools, and probably with anticipated future population growth will need more additional schools in future times. The history of the University of California and its schools of medicine is particularly interesting in this regard. For many years the University of California was satisfied to operate one medical school which is presently situated in San Francisco. The medical school at UCLA was opened shortly after the Second World War and has become a very strong and important institution. With increasing population pressure and increasing needs expressed by the State and its industries, there are now two additional medical schools being planned--one at Davis-Sacramento, the other at La Jolla-San Diego. There is a persistent rumor of a fifth medical school, this one to be a two-year medical school and situated on the Berkeley campus. You will note that this history reveals the firm establishment of one state university medical school of high excellence which serves as a model for subsequent additional increments when and where they may be needed. I firmly believe that the excellence of the initial medical school is of prime importance. If the first of the series of state-operated medical schools is anything less than the best, one may expect poor quality in the subsequent increments. If, on the other hand, the first school is truly superior, this is the model which all subsequent schools of the state university will have to follow. The investment involved may appear large, but it will bear returns for a very long time. The prospect of the State of New Jersey dotted with three or four medical schools of national renown operated by the state university is, I believe, the inevitable solution, and this solution can be achieved more promptly with the guidance and the assistance of your Commission.

I have drafted and redrafted this letter after a period of very deep concern. I thoroughly appreciate the problem which has been presented to your Commission and the superficially appealing solution of having Rutgers, in some way, "take over" the responsibility in Jersey City. To do so would be to make precisely those compromises with the concept of excellence in medical education which I had originally determined not to make. I clearly foresee among the consequences of such a "take-over" a continuance of mediocrity in medical education in the State of New Jersey which will be ever more difficult to overcome. Any of these proposals, should they be acted upon, would tarnish the ideals which my colleagues and I have

brought to our new venture in New Brunswick and would sadly depress morale. At an operational level, I am convinced that none of the proposals involving Rutgers University in Jersey City affairs are likely to work very well. I am therefore entirely satisfied with your rejection of our earlier proposal and trust that you will be willing to give thoughtful consideration to the ideas expressed in the latter part of this letter.

May I thank you and the members of your Commission for the courtesies which you extended to Dr. Denker and to me on June 8. I also welcome this opportunity again to present before you my own thoughts for what they are worth. I shall be happy to discuss any points which may be raised by these notes.

Very truly yours,

Dewitt Stetten, Jr.
Dean

Nevertheless, the committee did recommend to the State of New Jersey that it purchase Seton Hall Medical School. In support of my recommendation, Rutgers University declined to assume this medical school as part of its responsibility.

Belatedly, the committee, which had originally maintained that Jersey City was a splendid location for a medical school, decided that it had erred on this point and proposed that the medical school be moved to the metropolis of Newark, using as a major clinical facility Newark's large city hospital, called the Martland Hospital. It was noteworthy that this hospital was named after a distinguished research pathologist who had studied with enormous perseverance all the employees in a particular watch and clock factory after some of these died of osteogenic sarcoma. He found a considerable population to have been poisoned by radium to which they were exposed in the process of painting numbers on watch and clock faces with luminous paint. He discovered that all these employees were in the habit of "tipping" their paint brushes with their tongues, thus receiving very large quantities of radium paint into their systems.

The prospect for Rutgers Medical School at once looked dim. My advisor, General Robert Johnson, at about this point in time, suggested to me that I quit my position since under these circumstances it would probably prove difficult if not impossible to generate a first-class medical school in the state of New Jersey. The state was now possessed of two medical schools where a few

years before it had had none. It was clear that such support as the state might provide to medical education would probably favor the institution in the densely populated, ethnically disturbed, northern metropolitan area to the detriment of a school in semi-rural Piscataway. In my judgment, the state had clearly opted for the cheap, politically expedient solution to its problem, with little regard for the excellence of the solution. A letter from General Johnson to George Smith, dated July 31, 1964, is the best statement of the problem. How many copies of this letter were circulated by the General I do not know. But I do know that I received one. Following is the text of the letter:

Mr. G. F. Smith

This is a black day for New Jersey medicine. I have read with care your sales portfolio in support of Seton Hall offered to the joint informal session of the Legislature. I find it unfortunate.

The result of your Commission's work, thorough and tedious as it has been, is to have created a Catholic-Protestant situation, an unnecessary schism between the congested areas of Hudson, Bergen, Essex and Passaic counties with the remainder of the state, and sets the course for two possibly acceptable medical schools, but neither of the highest possible standard. Little degree of intelligence is required to forecast that in the years ahead the Legislature will apportion a certain maximum fund for medical schools, which through simple political arithmetic will be divided equally hence giving less than the full support required to either.

I am probably one of the few who conferred at length with Monsignor McNulty prior to the leased acquisition on the part of Seton Hall of the Jersey City Medical Center. I informed Monsignor McNulty at that time that it was not possible for Seton Hall to acquire the capital and to meet the annual deficits of a modern medical school. Now the record proves it. It was and is my view that Seton Hall should be phased out, fulfilling the moral obligation to its present students.

There is one basic objective in the field of medicine. It is "service to the patient." Having spent my life in affiliation with hospitals throughout the world I am confident that our best contribution to New Jersey medicine, and hence the patient, is the creation of one fine medical college. This of itself is a large and complex undertaking. Geographically its best location is New Brunswick. Little foresight is required to look forward to the next fifty years placing New Brunswick not only close to the geographic center of the state but close to the center of population.

I fear that your solution will be popular with the majority and hence I consider the book closed. I shall make no personal effort to oppose the conclusions of your Commission nor to advocate what I believe to be the proper course of procedure. I do not wish this letter circulated nor given publicity.

I shall continue my enthusiastic support of our four local hospitals in New Brunswick and I shall work closely with the hospitals in the Raritan Valley. Incidentally, the hospitals of the Raritan Valley offer a New Brunswick medical school good clinical material.

R. W. Johnson

In retrospect, I firmly believe that had the liaison committee and the Association of American Medical Colleges taken a more forthright stand in this situation and revealed, at least in substance if not in detail, what it had found on its several site visits to Seton Hall Medical School, the situation could have found a much happier solution. Whereas visits by the liaison committee were usually made to each school every five or more years, the deep concern which this committee felt toward Seton Hall Medical School is revealed by the fact that it paid visits to that campus in August 1951, March 1955, November 1956, February 1958, December 1959, March 1962, January and October 1963, March and September 1964, March 1966, May 1967, February and July 1968, March 1970, and November 1971. Clearly, this was a school with a serious accreditation problem.

It is of interest that as these events were concluding, there belatedly appeared a "white paper" (March 10, 1965) from the president of Seton Hall University, Bishop Dougherty. The substance of this revealing report was essentially in concordance with my own stated contention. Bishop Dougherty admitted that the medical school was not very good, that it was both politically and financially a burden upon Seton Hall University, and he therefore was determined one way or another to divest himself of the school. In this, of course, he succeeded. The text of the "white paper" on the transfer of Seton Hall College of Medicine and Dentistry to the state of New Jersey is reproduced below.

Events brought to light in the past six months and actions culminating in the passage of a bill enabling the State of New Jersey to acquire and operate the Seton Hall College of Medicine and Dentistry have prompted the issuance of this statement on behalf of Seton Hall University and the Trustees of the College of Medicine and Dentistry.

On December 22, 1964, Governor Hughes signed into law a legislative act which provides for purchase by the State of New Jersey of the Seton Hall College of Medicine and Dentistry. It is expected that a formal contract to complete the transfer will be executed at an early date. The Seton Hall College of Medicine and Dentistry will then cease to exist and will be succeeded by the New Jersey College of Medicine and Dentistry. The new institution will be under the complete control of the State, without affiliation or other relationship with the University.

The Seton Hall College of Medicine and Dentistry was incorporated as a legal entity separate from the University in August 1954. Two years were spent in constructing physical facilities, selecting a faculty, and making other necessary preparations, and the first students were admitted in September 1956. At that time New Jersey was unique among states of comparable population and resources in that it had no facilities for the education of physicians and dentists. The need for such facilities was clear, pressing, and immediate, and had long been recognized as a major hindrance to the future progress of the State. To meet this need the founders of the new institution gave of themselves with singular courage, devotion, and zeal.

The authorities of the Archdiocese of Newark and of the University had sought the counsel of outstanding experts in medical and dental education and were thoroughly aware of the magnitude of the task they were undertaking. They had no illusions as to the obstacles which might beset them. Nonetheless they remained steadfast in their determination to pioneer in giving New Jersey its first college of medicine and dentistry. It was with no small measure of pride that Seton Hall conferred the first medical and dental degrees in 1960.

Realistic as their appraisal of the situation had been, the founders of the new institution were confronted from the very beginning with difficulties and hardships which went far beyond what could have been reasonably expected. A series of harassing lawsuits, which required years of litigation for final resolution, challenged their every step; some financial support which had been expected and, in some instances, actually promised, was not forthcoming; support from some professional societies was either withheld entirely or only grudgingly proffered.

Despite these circumstances the College was able to make a remarkable beginning. A notable faculty of national stature was attracted to the new institution. The entering classes, selected from a very large number of applicants, were of high caliber, and their accomplishments at the College left little to be desired. As an official of the Council on Medical Education of the American Medical Association has affirmed, the College of Medicine, although a new institution, attracted medical students of excellent quality. The same official pointed out that, as measured by comparative scores on the examination given by the National Board of Medical examiners, the preparation Seton Hall medical students have

received is, in every way, comparable to that provided by long-established schools throughout the country.

Achievements of our dental students have been equally gratifying. In the National Dental Board Examinations our students have maintained an enviable record, with particular excellence in the clinical sections of the examinations. The accomplishments of alumni in internships, residencies, research, and professional practice provide further evidence of the high standards to which the College has adhered since its inception. As the academic reputation of the College thrived, so too did the program of faculty research, that is pure scientific inquiry, grow and receive wider recognition.

Under more fortunate circumstances, the Seton Hall College of Medicine and Dentistry might well have continued to produce superior graduates and, as a private institution, to make a major contribution to the welfare of this State.

It is true that the College incurred large deficits; it had been expected that it would. What had not been expected was that a more substantial measure of philanthropic assistance from the outside would not materialize. Yet, heavy as these financial burdens were, it is entirely possible that ways could have been found of bearing them and of continuing the College under private auspices if other considerations had not made such a course of action impossible.

A primary element in medical education is, of course, the clinical training which students can receive solely at the bedside in hospitals. This experience can be provided satisfactorily only if the professional services in the teaching hospital are under the direction and control of the medical school. This fundamental principle necessitates the utmost cooperation between the hospital and the administration and staff of the school. We have been forced to face the fact that the responsible authorities of the Medical Center and of the City of Jersey City have consistently failed to give this essential cooperation to the College-- cooperation which had been pledged and, to a large degree, formally contracted for.

Over the years the College has striven energetically and patiently to remedy this situation and to effect some workable relationship between City and school. When our best efforts failed, we were impelled to the conclusion that no acceptable solution was attainable. Consequently, in planning the future course of the Seton Hall College of Medicine and Dentistry, the Trustees had to choose from among the following courses of action:

- 1) To close the College entirely. This would mean the sacrifice of the significant progress which has been made despite all harrassments and would terminate the contribution of the College to the health services of the State of New Jersey.
- 2) To compromise the basic principle of professional control of

clinical experiences by the medical school, and to continue

to operate the College under its present limitations. This could be done only at the expense of the excellence which has been the school's hallmark up to the present time. The Trustees were unwilling to entertain such a solution.

- 3) To abandon the present facilities and to relocate the College at a new site. This would involve expenditures for construction of vast sums of money which, in the light of past experience, the Trustees could not reasonably expect to obtain from any non-tax-supported source.
- 4) To permit the State of New Jersey to take over the operation of the College. This preserves the advantages accruing to an established institution and ensures for the people of the State the continuing benefits of medical and dental education.

The Trustees were agreed that no alternative other than the last was acceptable.

This course of action assures continuity in the course of study already begun by the present students; it preserves the excellent faculty the school has attracted, and it maintains in New Jersey a source of physicians and dentists.

It is needless to say that the Trustees reached this conclusion with reluctance and regret. It should be added, however, that this regret is tempered by some pride and an awareness of the accomplishments of the Seton Hall College of Medicine and Dentistry:

- o Through its investment of time, talent, effort and money, it pioneered in making possible the first college of medicine and dentistry in this State.
- o It educated more than 400 physicians and 200 dentists.
- o It has given New Jersey a ten-year advantage in the establishment of a state-wide system of medical and dental education.
- o It has made this school available to the State at a great financial sacrifice and at a small fraction of what it would otherwise have cost the taxpayers.

The Trustees of the Seton Hall College of Medicine and Dentistry congratulate Governor Hughes, his distinguished committee under the chairmanship of Mr. George F. Smith, the members of the Legislature, the press, and all citizens of New Jersey that this work so well begun and so effectively advanced will continue to inure to the benefit of New Jersey residents.

/S/

John J. Dougherty
Auxiliary Bishop of Newark

President, Seton Hall University

Meanwhile, other clouds were gathering. Because of the growth of the college and university system which the state was now supporting, a determination was made to separate an Office of Higher Education from the preexisting Office of Education. To direct this new office, Ralph Dungan was selected as Chancellor. Dungan, when asked his profession, quite candidly stated that he was a "pol." He had served on the staff of Senator John Kennedy and subsequently had been named Ambassador to Chile. He had left this position hurriedly when it was averred that he was serving the CIA. He was selected as Chancellor of Higher Education in the State of New Jersey, a position to which, in my opinion, he brought remarkably few qualifications. He had all the charm which one associates with a politician of the so-called "Irish Mafia," but his credentials in the field of higher education were not impressive. He and Governor Hughes had gone, I believe, to the same parochial school in Pennsylvania; later he spent a year at the Woodrow Wilson School of Princeton University. He now became an instant expert in medical education and, I must suppose, in all other phases of higher education. We had been developing architectural plans for our teaching hospital. On one occasion when these were up for review by the appropriate Federal agency, Chancellor Dungan chose to criticize the plan acrimoniously in a fashion which revealed to me that he truly knew very little about the planning of a modern hospital. It was in his office that the scheme was ultimately developed to separate Rutgers Medical School administratively from Rutgers University, and to blend it with the school in Newark under the name of the Medical and Dental Colleges of the State of New Jersey. This new amalgam was to have its own president, its own board, and its own budget. This proposal caused deep dismay to my faculty, to my students, and to me. It represented a breach of all of the assurances that I had been given when I moved to New Brunswick. It meant that my students, upon graduation, would not receive degrees from Rutgers University. It would separate the medical school from an appropriate university sponsor, a relationship deemed of great importance ever since the report of Abraham Flexner in 1910, and marry it to what I well knew to be a medical school of very undistinguished character. It appeared to defeat my efforts to bring excellence to this new institution and to the state of New Jersey. With no dissenting vote, all the members of the faculty and of the student body joined me in a vain attempt to defeat this new plan.

By this time, the Democratic Governor Hughes had retired and was succeeded by Governor William Cahill. Governor Cahill's strength in the Republican Party rested in part upon the fact that he had led the Republicans from New Jersey in the convention which nominated Richard Nixon for the Presidency. It was, in fact, Cahill's action which put Nixon over the top as presidential candidate. I met with Cahill only twice. On one occasion he and members of his cabinet visited our medical school to receive a briefing on our budget request. He challenged my projection as to the size of faculty which would be required to cover all the materials that had to be presented to medical students. Using as a model the "Little Red Schoolhouse," he asked why members of the Rutgers Medical School faculty could not spend substantially full time in teaching medical students. In vain I tried to explain to him that members of medical school faculties have many other tasks and responsibilities: they must take care of patients; they are expected to conduct research (there is that wicked word again--substitute "investigation"); and above all, they must perform as scholars in order to be qualified to serve as first-class teachers. These activities interested Governor Cahill not at all. He commented that he was not opposed to research, but he saw no reason why it should be conducted by faculties of medical schools. He saw in our plans an attempt to create a Harvard Medical School on the Raritan and objected to the fact that so many of our two-year graduates completed their medical training at Harvard. He told me that New Jersey did not need doctors such as were produced at Harvard; what it needed were doctors who knew how to take out tonsils. I realized that it would be futile to explain to this Governor that New Jersey already had a plethora of that kind of doctor. He suggested drastic reductions of faculty-to-student ratio, and when I protested that we might lose our accreditation under such circumstances, he responded, Who needs accreditation? I am a graduate of a non-accredited law school, and look at me." I bit my tongue to avoid making the obvious response.

Dungan, the Chancellor of Higher Education, and Cahill, the Governor, although of opposite political parties, worked together very closely. Legislation was drafted which would effect the scheme that Dungan had devised and would forever separate Rutgers Medical School from Rutgers University. Every member of the faculty and of the student body undertook to do what he could to lobby against this proposal. Finally, a hearing was held in the Legislature in Trenton at which Mason Gross, John Cooper, President of the

Association of American Medical Colleges, Carl Kaysen, President of the Institute for Advanced Study at Princeton, and I were witnesses. Cooper failed to divulge any of the adverse information which his association had garnered on the subject of the Seton Hall Medical School. Kaysen's expertise seemed to derive chiefly from his participation in a study run by the Carnegie Foundation on Higher Education. I personally found him poorly informed in matters of medical education. Mason Gross argued for the integrity of Rutgers University, and I argued for the continued intimate connection between Rutgers Medical School and Rutgers University. I then returned to New Brunswick. We had a class of medical students to graduate and we had our fine new building, now completed, to be dedicated. I had invited Philip Handler, who had become President of the National Academy of Sciences, to come up from Washington to speak at the dedication.

I was interested in the intensity of the reaction of the medical students. We had, of course, taught our students a good deal of genetics. Some of them took it into their heads to consider what would happen if one hybridized a Dungan with a Cahill. Clearly one of the possible hybrids would be a Dunghill, and cartoons of this strange chimera started to appear on the bulletin boards of the medical school. All the faculty and all the students actively participated in a lobbying effort: calling upon legislators and citizens, securing signatures to a petition opposing the projected change, and seeking support for our cause wherever there was any likelihood of success. I may say that the performance of the board of governors of Rutgers University was disappointing. I believe that a strong statement on their part might have been heeded, but none was forthcoming. Mason did address the university faculty on one occasion in support of our continued participation in the university, but to little avail. I let it be known among friends and colleagues that I had little interest in continuing with the medical school if indeed it was to be severed from Rutgers University.

On June 8, 1970, New Jersey's Senate approved the action of the Assembly to sever Rutgers Medical School from the university and put it under a new administrative arrangement heavily weighted in favor of the Seton Hall College of Medicine and Dentistry. The New York Times a day earlier editorialized:

Doctors on the Cheap?

New Jersey has long been a disaster area so far as medical education is concerned. It has so few medical school facilities

that the overwhelming majority of its young people who would become physicians must go elsewhere for their training. Its resources for graduate medical education are so unattractive that, as Gov. William T. Cahill pointed out last month, the state's hospitals can fill less than 75 per cent of their intern and residency vacancies, and then only by relying overwhelmingly on foreigners. Yet by any criterion New Jersey is one of the nation's wealthiest states.

Since Gov. Cahill says he is concerned about this situation, one might expect him to be leading a campaign for vast expansion of medical training in his state, giving additional funds for that purpose a very high priority in his budget. On the contrary, his present position seems to be that New Jersey can train more good doctors by cutting planned expenditures in this field, and by abandoning the idea that medical education and medical research have anything in common. He has repudiated his predecessors' pledge to build a strong second medical school for the state at Rutgers. Moreover, by the use of appropriate political arm twisting, he is attempting to have the state Legislature sever Rutgers' existing two-year medical school from the university and put it under a new administrative arrangement heavily weighted in favor of the old Seton Hall College of Medicine and Dentistry.

Academic administrative arrangements can always be debated: but the tone of the Governor's message to the Legislature last month must arouse the greatest concern. His dream is of training doctors on the cheap, and his gibe at those who think that "only academic geniuses can become doctors" suggests he believes one need not be overly concerned whether medical school students are intelligent. It is hard to escape the conclusion that the Governor's real motive is to spend as little as possible on medical education.

Mr. Cahill's tactics of trying to railroad his proposals through without anything resembling adequate discussion suggest that he fears the consequence of public understanding of what he is trying to do. New Jersey's Senate will probably vote on the Governor's bill on Monday. In the interests of the state the measure should be defeated.

Clearly, Cahill and Dungan were professionals, while my colleagues at Rutgers Medical School and I were the rankest amateurs in the political process. It was disappointing but not surprising that we were defeated. Two days after the vote I submitted my resignation as Dean of Rutgers Medical School. By this time, several of my colleagues on the senior faculty had already become discouraged and had left. Clifford Gurney had gone to the University of Kansas, and his successor, Bill Wilson, decided to leave academic medicine and return to his favorite state, Maine, in private practice. Gerhard

Plaut, my chairman of biochemistry, accepted an offer at Temple, and Al Silverman, chairman of psychiatry, moved on to the University of Michigan. Before my resignation I had explored possible opportunities for employment at the National Institutes of Health and was gratified to find that I would be most welcome. There was some delay in completing my appointment, apparently brought about by a hostile telephone call from Governor Cahill's office to his cronies in the White House, but this delay lasted only a couple of months.

My stay in New Jersey gave me an excellent opportunity to observe the nature of corrupt state politics. During the period while I was in residence in New Jersey, I saw one after another of the major political figures in that state accused, indicted, and not infrequently convicted of serious crimes. Of the officers immediately surrounding Governor Cahill--his Secretary of State, his Secretary of the Treasury, his Attorney General, and his chief political officer--all came under serious scrutiny by the law. In fact, the New York Times on its front page published a summary of the history of corruption in the state government of New Jersey and collected between 50 and 60 names of prominent state officials who had at that time either ended up in jail or had come under scrutiny of the Federal prosecutor. Even in a state accustomed to corrupt government, the Cahill administration apparently proved unpalatable and Cahill was denied the opportunity to run for a second term by his own Republican Party. My observation of the Cahill Administration in Trenton was an excellent prelude to my subsequent observations of the Nixon Administration in the early 1970s. The very same administrative arrogance which led to Watergate and the downfall of Richard Nixon in the Federal Government was abundantly evident in the regime of William Cahill and his friends. As I watched the Washington Post for the latest developments in Watergate, I had a sense of *deja vu*.

In retrospect, a number of factors can be identified which led to the relegation of my promising Rutgers Medical School to second class status for many years to come. Had the Association of American Medical Colleges waived its normal secrecy and revealed to the appropriate authorities all that it knew about Seton Hall Medical School, the legislative actions binding that school to Rutgers Medical School would probably not have ensued. Had the governors of Rutgers University taken a firm stand, demanding that Rutgers Medical School remain as it was conceived, a part of their university, Rutgers Medical School would more rapidly have become a flourishing academic medical center. As things now stand, Rutgers University must remain one of the relatively few

great state universities which lacks a medical school. As such, it is in my judgment an incomplete state university, and as far as I can foretell is likely to remain so. Medical schools, it should be recalled, are not a recent addition to the corpus of the university. In fact, the earliest of universities--at Salerno--is remembered as an institution of medical education.

My experience at Rutgers was in many ways the most exciting episode in my life. It was also the most frustrating. The accumulating frustrations undoubtedly contributed to a myocardial infarct I suffered in 1965 and which left little residual damage.

In retrospect, I have found little reason to change my fundamental ideas about medical education. I still believe that the best place for a medical school is administratively and geographically on the campus of a great university. I still believe that the clinical departments--namely, the hospitals and outpatient services, must be situated if possible immediately adjacent to the basic science departments, and that the best teachers are those participating in and familiar with the latest research developments. I furthermore believe that the educational process must operate essentially totally independently of the political process.

Persons involved in higher education, particularly in professional education, are often charged with elitism. I, for one, am unabashedly elitist. I can see no other way. What I teach and what my students learn is for the carefully selected few; and we, the relatively few who have some understanding of what we are doing, must be given authority to do it as we see fit. Outsiders can inspect and may comment but their contributions will necessarily be limited. Legislatures and governments may support or not support ventures in medical education. The planning and the operation of the venture, however, must be left in the hands of the academic physicians, the medical scientists, and the medical teachers who alone know what it is all about. Any other course, in my experience, will most certainly lead to disaster.

When Rutgers Medical School was in its very early years, our school ranked fifth among the approximately 120 schools of the nation in scores achieved on national boards. By the time Chancellor Dungan and Governor Cahill had finished with us, the College of Medicine and Dentistry of New Jersey ranked, on a recent evaluation study by scholars of Columbia University, at the very bottom of the list. To such depths had we fallen.

Chapter XIII

GENERAL MEDICAL SCIENCES

In the spring of 1970, the Federation of American Societies for Experimental Biology met, as it frequently used to meet, in Atlantic City. This was prior to the time that Atlantic City entered the gambling business and hotel rates were still within the reach of biologists. Affairs at Rutgers Medical School were deteriorating as a result of the action of Chancellor Dungan and Governor Cahill, and I recognized the possibility that I might soon be seeking other employment. It was on the boardwalk at Atlantic City that I ran into Bob Marston, then director of NIH. He greeted me warmly and at once proposed that I consider returning to Bethesda. Although he made no mention of any particular job, I was naturally delighted by this friendly reception: and when a few months later the Legislature at Trenton voted to sever Rutgers Medical School from Rutgers University, I had no hesitancy in calling upon old friends in Bethesda to explore what opportunities might have developed.

The early institutes that were put together as the National Institutes of Health were conceived as categorical institutes. Their names reveal what was meant by "categorical": the National Cancer Institute, the National Heart Institute, the National Institute of Arthritis and Metabolic Diseases, the National Institute of Neurological Diseases and Blindness, the National Institute of Dental Research, the National Institute of Allergy and Infectious Diseases, and so forth. There was, however, a considerable body of health-related research which did not conveniently fall into one or another such category. In order to provide for support of such research, which was housed largely in the basic science departments of the several medical schools, the Division of General Medical Sciences had been established and its guidance was entrusted to Dr. Frederick L. Stone. After a few years this division was promoted to the level of an institute--the National Institute of General Medical Sciences (NIGMS)--and it was the major source of research support to departments such as biochemistry, physiology, anatomy, and pharmacology. Under Fred Stone's guidance its budget grew rapidly, and then abruptly Fred decided to leave Bethesda to assume the presidency of New York Medical College. A couple of years earlier my friend from Rutgers, David Denker, had left to assume this

very job, but his views of medical education, which I suspect he had acquired in good course from contacts with me, were not compatible with those of the faculty and board of trustees of this medical school. It was to succeed David that Fred Stone left Bethesda, thus creating a vacancy which was now offered to me. I accepted with alacrity, since my deepest interests in medical research were related to the activities of the basic medical science departments. My only important disappointment was that NIGMS, a late comer among the institutes, had no laboratory or clinical research space and therefore had no intramural program. My own familiarity with NIH had up to that time been predominantly with the intramural scientific activities.

In addition to supporting research grants in the basic sciences in virtually every medical school in the country, NIGMS was also the chief source of support for pre- and postdoctoral fellows at various levels of their training. The very large fraction of the funds spent by NIH in fellowships, research career development awards, and training grants funneled through NIGMS. Of particular interest to me was a program recently introduced in 1970, entitled the Medical Scientist Training Program, which underwrote the costs of training a limited number of gifted students both in medicine and in research in a basic medical science. This normally took the candidate seven or more years to complete, and at the end of his training he would receive both the M.D. and the Ph.D. degrees. It was expected that the graduates of this program would spend most of their professional lives in academic medical institutions, teaching future generations of medical students and conducting sophisticated research. This was to be the training ground for much of the next generation of academic physicians. The program was the pride and joy of Drs. Vincent Price and Leo von Euler at NIGMS.

I spent the summer of 1970 with my family in our home at Woods Hole, awaiting word from John Sherman and Bob Marston at Bethesda that my appointment as director of NIGMS had been processed. The delay was the result of a futile attempt on the part of an embittered Governor Cahill, of New Jersey, to try to scotch my appointment. To this end he apparently consumed some of his residual influence with the Nixon White House. Happily he was not successful and my appointment was finally forthcoming. It was an important year in the history of NIGMS because in the hearings before the appropriations committees of the House and Senate, testimony was given by an old friend, Joshua Lederberg, at that time professor of genetics at Stanford Medical School. Josh had been a

medical student at P & S many years earlier. I remember that he presented a problem to the Department of Biochemistry. While unquestionably brilliant, he rarely attended either the lectures or the laboratory exercises, and we were in a sense relieved when he left P & S to work toward his Ph.D. degree at Yale University. It was while there that he made his important contributions to the sexual life of Escherichia coli, which earned for him not only his degree but also a Nobel Prize. He had become one of the leading figures in the extraordinary development of the science of genetics, and in his Congressional testimony he argued extremely effectively for the support of programs that would bring modern genetics together with clinical sciences. He advocated the establishment of a number of genetic centers at several medical schools, each center to contain both clinical and basic science activities. To this end he requested an increment of \$10 million, and remarkably the Congress accepted this recommendation in detail. These funds were to be made available predominantly to NIGMS. I spent much of the summer of 1970 considering and discussing with acquaintances at Woods Hole the best means of using these additional funds.

Our domestic move from New Brunswick to Bethesda was complicated by the fact that George, our youngest, was about to enter his senior year of high school. We had made the mistake in an earlier move of displacing our daughter Nancy for her senior year--an emotionally traumatic year, since it is during that time the students learn of their success or failure in the process of college admissions. We therefore decided to retain our New Brunswick home while I commuted back and forth to Bethesda. Each Monday I would proceed by rail from New Brunswick to Washington, returning on Thursday or Friday afternoon as the workload permitted. Marney, meanwhile, maintained the New Brunswick home, and George continued to attend the Rutgers Preparatory School from which he graduated the following spring. Domestic arrangements in Bethesda were simplified by the fact that NIH was able to make available to me one of its "general officers' quarters," one of a limited number of very satisfactory small homes of an architectural style which in Britain is called "semi-detached." By this I mean that two such private homes were constructed under a single roof, and it happened that we shared this roof with Herbert and Celia Tabor. These were very old friends of ours, Celia Tabor having been Celia White, a medical student of mine at P & S and a dormitory mate of Marney's at Bard Hall. Herbert Tabor was chief of the laboratory of chemical pharmacology at the National

Institute of Arthritis and Metabolic Diseases. My oldest daughter, Gail, by this time married to Peter Maloney, was working toward her Ph.D. in genetics at Brown, while Peter, who had completed his Ph.D. training in microbiology, had secured a position at Walter Reed Army Medical Center to fulfill his military obligations. The Maloneys moved into our new home and kept house for me during my stays in Bethesda. It all worked out very comfortably, although I found the weekly commutation to be fatiguing. Soon after George's graduation and his move to Harvard, we vacated our New Brunswick home and Marney moved in. The Maloneys had by this time made their own postdoctoral arrangements, Gail in the pediatrics department and Peter in the physiology department at Harvard Medical School, and once again the Stettens settled in at Bethesda. Marney was assigned a position in our old section on the ninth floor of the Clinical Center, which was now run by our old colleague Yale Topper. My former office of scientific director of NIAMD was very effectively occupied by my old friend Ed Rall.

Since NIGMS had no intramural activities, its staff was housed off campus in a large rental property called the Westwood Building, situated some distance from the main campus. I found this to be an unhappy environment and was therefore pleased when Bob Marston determined that all institute directors should have offices on the campus. I was provided with office space in Building 31 and soon moved in.

Among the delightful people with whom I worked at this time was Gordon Klovdahl, Executive Officer of NIGMS. With this large and smiling man I immediately hit it off. The Executive and Administrative Officers of NIH fall into two classes. There are those who are thoroughly familiar with all the rules, regulations, forms, and procedures and who, when confronted with a problem presented by one of the scientific staff, can always find some rule or regulation making accomplishment of the assigned task either illegal or otherwise impossible. There are others, however, who while equally familiar with the regulations find in each new assignment a challenge. How can the rules be bent in order to permit us to proceed? Are there ways of achieving the desired goal which circumvent obstructive regulations? From the point of view of the scientific director, it is the latter type of executive officer who is to be preferred. Gordon Klovdahl's greatest joy in life was to receive a difficult assignment from me or from others of the scientific staff and to find some way --perhaps, occasionally, an unorthodox way--of accomplishing the desired

purpose. Usually he would tell us how he had accomplished his purpose, but on occasion he would smile and say, "It's too complicated to explain." Contracts, promotions, and appointments moved expeditiously through Gordon Klovdahl's office and were always treated with ebullient good humor seasoned with moderately salty jokes. I have had contacts with many executive officers both before and since, but none has given me greater pleasure than Gordon. He had served as a medical corpsman in the Navy during World War II and had used his veterans' benefits to secure college training. He lived in a meticulously maintained home in Wheaton, Maryland, surrounded by a devoted family, which included two daughters and a fascinating adopted Korean granddaughter. In his basement game room he maintained a complete file of Playboy magazine.

At NIGMS, I renewed friendship with Dr. Vincent Price, who was trained as a physician. Vince had come to the National Cancer Institute to work in the chemistry laboratory of Jesse Greenstein, where he participated in the early enzymatic resolution of dl-amino acids. He had long since entered the ranks of the scientist-administrators and was now busily stimulating grant-supported research programs. He had a particular interest in the Medical Scientist Training Program of NIGMS but he was always available to any applicant who needed advice or assistance in procuring support for any worthwhile research project. Vince is, bar none, the most generous man I have ever known. He is not only generous with material things, distributing gifts among his many friends, but what is more important, he is generous of his time and his affection. Whenever disaster strikes, as when a member of the staff takes sick and must be transported home, or when an auto breaks down and transportation is needed, Vince will always be on hand ready to assist. Curiously, one never has to call him to tell him of such a need. Through his own peculiar channels of communication, he always seems to know and promptly appears to offer his assistance.

Vince is happily married to a medical school classmate, Florence. From time to time, the Stettens and the Prices join forces of a Saturday or Sunday to inspect a local azalea garden or to visit a favored apple orchard. Vince always purchases numbers of bushel baskets of apples which he then distributes among his friends.

Perhaps my most engrossing assignment was to maximize the yield of science to be derived from the \$10 million increment that we had secured from the Congress. A number of genetic centers were established on major medical school

campuses, such as those at San Diego, San Francisco, and Seattle. Of particular interest to me was the establishment of a working collection of mutated human cell lines. Because I had given birth to this idea myself, I was particularly happy to see it blossom. After much consideration a contract was finally awarded to the Institute for Medical Research in Camden, New Jersey, headed by Lewis Coriell. Cell lines were soon accumulated from many sources, each colony coming from a carefully studied patient with a recognized and diagnosed genetic defect. The purity and identity of the culture were confirmed by Dr. Coriell and his associates and the colony was then amplified. Cells were placed into 200 ampules and these were frozen under liquid nitrogen. As the collection grew, a special building had to be constructed to house the ever-increasing number of deep-freeze chests. As of last reading, there were about 3,000 lines of cells in the collection. Each year approximately 3,000 solicitations are received from scientists all over the globe, and to each legitimate request an appropriate ampule of frozen cells is dispatched. The overwhelming majority of such mailings results in the satisfactory growth of the required cell line. In this way a very diverse collection of cells is immediately available to any investigator, and many investigators in different parts of the world can confidently perform experiments on what are bona fide clones of one and the same cell line. The collection in some ways serves as a cell library, and in other ways as a cell bank. Because Lew Coriell and his colleagues are technically extremely skilled and demanding, the cell lines are kept free of bacterial or other contamination in contrast to many other cell culture laboratories. Dr. Coriell does not permit the use of antibiotics to suppress the growth of bacterial contaminants. Each year he publishes an increasingly impressive catalog giving a great deal of information about each cell line. It is worth recording that for each of the 23 chromosomes in the human karyotype, this collection now has at least one genetic marker. Needless to say, this collection has proven invaluable in the mapping of the human karyotype. From the users of this library of human cell lines I hear only enthusiastic praise, particularly from those scientists who are actively engaged in the mapping of the human karyotype.

The process by which the agencies of the Federal Government obtain their appropriations is a curious one and by my observation not generally understood by the citizenry. The President normally presents to the Congress a State of the Union message in January of each year. One or two weeks thereafter he

presents his budget message, which contains the President's asking budget for the following fiscal year. The pieces of this budget are then distributed among the subcommittees of the budget committee of each chamber, and hearings commence. The fiscal year formerly ran from July 1 to June 30. It now runs from October 1 to September 30. One might suppose that during the interval January to July, or January to October, the Congress would have ample time to act upon the President's acting budget and submit an appropriations bill. This, however, happens very rarely. Usually, when the new fiscal year begins (and each fiscal year is named for the calendar year in which it terminates), the work of the Congress is far from complete. Then in a great hurry it passes a continuing resolution to permit the business of Government to continue without major interruption. If it fails to do so, then the agency which is without appropriation cannot conduct business, and indeed everything--including paychecks--is interrupted. Usually well into the fiscal year an appropriations bill is finally passed and signed. Even then, the funds that have been appropriated are not necessarily guaranteed to the agency. The Office of Management and Budget acts as a paying teller to the Office of the President and releases, or on occasion fails to release, appropriated funds, sometimes causing grave distress in the affected agency and among its prospective grantees.

The budget process is a continuing one. During each summer the institutes start assembling information for the budget to be followed 18 months later, considering all their anticipated future needs. These in turn are discussed with the director of NIH, who must adjudicate the normal competitive differences between the several institutes. The NIH is but one of six major components in the domain of the assistant secretary for health, and he is but one of several components in the office of the Secretary of Health and Human Services. The Secretary, although he might appear to be a powerful person, is subject of course to the wishes of the President, as these may be transmitted either directly or through the agency of the director of the Office of Management and Budget. This office, which is instrumental in preparing the President's asking budget, in effect assigns ceilings to each department of Government and sometimes down to the agencies and bureaus. This information filters back to the directors of the several institutes during the late fall, and provisional budgets are drafted to conform to these figures. This information from all agencies of Government is assembled in the Office of Management and Budget, which then provides the President sometime in December

with the fact document, "The Budget of the United States," which is the basis of his budget message to the Congress. It often happens that one must design a budget at a time when one is quite uncertain not only what one will have in the previous year but what one has for the year in which he is preparing the future budget.

One of the most challenging jobs that falls to the director of an institute of NIH is the defense of his budget before the appropriations subcommittees of the Congress. In my time, the House appropriations subcommittee before which we testified was chaired by Congressman Daniel Flood of Pennsylvania, while the corresponding Senate subcommittee was chaired by Warren Magnuson of Washington. Each institute director makes extensive preparations for this event since he may receive questions on any and all aspects of the activities of his institute. He sits at a table surrounded by his top staff, including his executive officer, his deputy, and others, and faces the committee. A written statement is carefully prepared and this is read to each committee. After that, the free-for-all commences and this can be either good clean fun or a miserable experience, depending upon the attitude of the committee and its chairman. Daniel Flood, who has since retired from the Congress under a cloud, was an excellent committee chairman. His earlier activities had included a spell on the stage, and there was much melodrama in his makeup as evidenced by his extraordinary waxed mustaches and the opera cape which he affected. He liked to quote from Shakespeare and very much resented any witness who tried to match him in this area. Each institute director was carefully coached to defend the President's asking budget and not to solicit additional funds. Such activity was termed "budget busting" and was frowned upon by the Secretary and his staff. To guard against budget busting, the Secretary would send one of his associates whose job it was to interrupt us should we try to bust the budget. Only on rare occasions was it permissible to indicate areas in which the President's budget seemed to us to be insufficient. This we were allowed to do in response to specific questions by members of the committee. The House appropriations subcommittee was generally well represented at those hearings which I attended, and after the chairman had asked all the questions that had occurred to him, each committee member was encouraged to continue the questioning. It developed that several members of this committee were curious about the nature of genetic disease, and I soon found myself in the role of instructor to a per-

ceptive class of Congressmen in the field of basic genetics. These lectures carried forward from year to year.

My appearances before Senator Magnuson were of quite a different nature. In the first place, whereas the House subcommittee met in a large, well-ventilated room in the House Office Building, the Senate subcommittee met in a very crowded, poorly ventilated room in the basement of the Capitol. Not infrequently Magnuson sat alone on his side of the table and did all the questioning. The House hearings usually preceded those in the Senate in conformity with the constitutional prescription that money bills should originate in the House of Representatives. The Senate hearings were often perfunctory. When, as sometimes happened, questions were asked that could not immediately be answered, the witness requested the privilege, which was always granted, of subsequently supplying an answer in writing. After each hearing we eagerly awaited the report of the hearing in the Congressional Record, and finally the action of the conference committee, which was invariably established to iron out the differences between the proposed bills in the House of Representatives and in the Senate. The conference report was generally accepted on the floors of both houses and the measure was then sent to the White House for the President's signature. During the four years in which I testified, presidential signature was forthcoming in three. In the fourth of these years, however, the bill as passed by the Congress was vetoed and we were funded on a repeated "continuing resolution," a Congressional action which awards to us a sum of money dictated by the prior year's budget. Since NIGMS is a noncategorical institute, it may have been slightly more difficult to convince the members of the appropriations subcommittees of the importance of the work which it supports. I was pleased that in each of the years when it was my job to defend our budget, the appropriation for NIGMS increased.

The development of a strong program in genetics by the institute fell chiefly to Fred Bergmann, a man of great intelligence and industry. He familiarized himself with all the applicants and their projects and kept me briefed on progress. We soon had eight genetic centers in operation and most of these proved very rewarding in investments. In other words, we put into effect the plan which Joshua Lederberg had sold to the congressional subcommittees. We sponsored activities in the field of amniocentesis and prenatal diagnosis, genetic counseling, mapping of the karyotype, and identification of genetically transmitted diseases. I have personally derived deep satisfaction

from the knowledge that my oldest daughter, Gail, who earned her Ph.D. degree in genetics and subsequently had a postdoctoral experience in human genetics, now serves as an assistant professor at Johns Hopkins Medical School, directing the cytogenetics diagnostic laboratory for the obstetrics and pediatrics services.

In 1972, Richard Nixon was relected to the presidency by an overwhelming majority and must have felt very sure of his political strength. He had finally overcome the humiliation that he must have experienced when in 1960 he had been soundly defeated by John Kennedy. In his exuberance, therefore, he collected letters of resignation from many agency heads. Such a submission of resignation is a frequent occurrence when there is a change in administration, and I believe that Bob Marston, then Director of NIH, never for one moment believed that his resignation would be accepted. After all, he had served well during the first Nixon administration and there had been no particular areas of conflict. It was Marston's style to govern the NIH by a triumvirate, sharing the responsibility with John Sherman, deputy director, and with Bob Berliner, deputy director for science. This was in contrast to the earlier style as practiced by Jim Shannon who dominated the NIH by his own political skills and the force of his personality. The trio of Marston, Sherman, and Berliner gave excellent governance to NIH and everyone expected that they would continue in their respective roles for a long time. Then abruptly the ax fell. For reasons that I never understood, Marston's proffered resignation was accepted. It was a shattering blow.

John Sherman assumed the role of acting director. Several months later, Bob Berliner, who had been deeply distressed by Marston's dismissal, accepted the post of dean of Yale Medical School and soon thereafter I was approached with the suggestion that I become the new deputy director for science. This was a purely administrative position with a major responsibility for the intramural scientific activities on campus. It represented for me a very considerable change, since at that time I was about 65 years old and was suffering from a significant progress in the macular degeneration which had been troubling me since Rutgers days. Therefore, I had some hesitancy. However, the prospect of new adventures in Building One was sufficiently intriguing and I accepted. I made it a condition of my move that my secretary, Mrs. Nancy Hawes, move with me to this new post.

This leads me to a discussion of the importance of secretarial support in the kind of work in which I have been engaged. I should like here to pay tribute particularly to my last three secretaries, all of whom have been women of unusual characteristics. When I moved to Rutgers in 1962, my very first appointment was that of William Hillis who served as business manager for Rutgers Medical School. My second appointment was that of Miss Enid Hirsch who became my secretary and later to my several successors in the dean's office. Enid was a good humored and intelligent woman who over the years has learned more about Rutgers Medical School than any other person I know. Enid has a mousetrap memory from which little if anything escapes, and she has made Rutgers Medical School her own. Only once during our eight years of daily contact did I see her lose her cool. This occurred when she was charged with a parking violation by the university police patrol. It was her contention that the altered parking rules were added to the signpost in such small print as to be entirely inconspicuous, and she therefore declined to pay the \$3 fine which was imposed. One day, by chance, there came to my desk a letter addressed to her containing the threat that she would be denied the privilege of parking on Rutgers University land if she did not at once remit \$3. In the hope of assuring myself of the continued services of an excellent secretary, I surreptitiously paid the fine myself. Some weeks later Enid discovered my invasion of her private arguments and she was furious at me. For the first and only time during those eight years of daily contact, tears welled in her blue eyes. I am happy to report that her anger was short lived.

When I moved to NIGMS I found Nancy Hawes, or rather according to the procedures of Federal employment, she was found for me by Gordon Klovdahl. She remained my one and only secretary throughout my next two jobs. Nancy had returned to the labor force after the death of her husband, and was the most remarkably precise and rapid typist with whom I have ever worked. Her spelling is all but infallible and her knowledge of the rules of punctuation is second to none. She turns out manuscript with speed and precision. Nancy has other talents. She earned her way through college in part by playing the piano in an all-girl dance band. As a result, she is always in great demand at social gatherings where she graciously sits down to the piano and plays any tune when asked, provided it dates back to the 1940s and 1950s. She does this easily and gracefully, and we have particularly enjoyed her performance when she plays four hands with my son, George, himself a very able piano player. Nancy took

particularly good care of me during the years of my decreasing visual acuity. There was a period of time when I could still read very large type. She discovered somewhere at NIH a typewriter that produced letters far larger than usual. With great consideration she transcribed on this cumbersome machine all of the talks I had to give. She also learned to go through the incoming mail and select those items which were most important for my work. As time permitted she would read these to me. Over the years she progressed to approximately the highest grade available to a secretary. When I left Building One for a more humble job, it was not feasible for Nancy Hawes to move with me.

In my present position as senior scientific advisor, I have been singularly fortunate to find another Nancy--Nancy Yellin. This Nancy is the wife of Dr. Herbert Yellin, a member of the staff of the National Institute of Neurological and Communicative Disorders and Stroke and himself a neurobiologist. Mrs. Yellin has been living around scientific laboratories for many years and is remarkably knowledgeable not only of the people who occupy these laboratories but also of the work in which they are engaged. Although she has little formal training in science, she attends with considerable profit most of the seminars and other scientific discussions in which I become involved. She has taken virtually complete charge of the scheduling of my seminar series and has proved of great value to me in the other duties that I am presently carrying forward. To be the secretary of a blind man is clearly not an easy chore, yet Nancy Yellin attacks this job with unfailing cheerfulness and good will. She is the mother of five children of assorted ages over whom she worries like a mother hen. I suspect that subconsciously she includes me among her children.

One of the functions of each institute director is to work closely with his national advisory council. These councils were set up by law and they include a number of influential and interested lay persons. Their concurrence is required before any grant can legally be funded. During my tenancy at NIGMS, council meetings, which occurred twice yearly, were usually fairly mild and peaceful events and I shall not devote time to them here. I should, however, like to mention one council member who was a remarkable person. This was Marjorie Guthrie, widow of Woody Guthrie, the great folk singer and guitarist, and the mother of Arlo Guthrie. It will be recalled that Woody Guthrie died a number of years ago as a result of Huntington's chorea, a very destructive disease of the central nervous system which is genetically transmitted as a dominant. Because of her concern with this disease of her late husband and

with her children, Marjorie Guthrie founded the Committee to Combat Huntington's Disease and served for many years as its president. She had become thoroughly familiar with the vagaries of Huntington's disease. She had met many of the families that carry this unfortunate disease, and she had done a great deal of lobbying in and about Washington to secure funds for research in this area. Marjorie, although of small size, is a very commanding person and had no hesitancy in calling on Senators and Congressmen to tell them of her cause. She early recognized the advantage of making the attack on a broad base--that is, an attack on all genetically transmitted diseases, rather than staging an isolated war against Huntington's chorea. Marjorie had been a dancing teacher in early life. She mastered the guitar during her husband's illness so that she could transmit this skill to her children. She was a very refreshing member of the National Advisory General Medical Sciences Council and the only member who always greeted the Director of that Institute with a cheerful "Hello, dearie" and with a kiss on the lips. I continue to hear from her from time to time. Her little notes are always signed, "Love and Peace, Marjorie."

On our return to Bethesda in 1970, Marney was provided with a position, an assistant, and a laboratory module in the very same section in which we had earlier been employed. Our old colleague, Yale Topper, continues as chief of this section, and Marney continues to produce interesting papers dealing chiefly with certain enzymes of the mammalian liver and of the related hepatopancreas of crustacea.

Chapter XIV

BUILDING ONE

There was deep distress in the Office of the Director, NIH, in 1973. Bob Marston had been summarily dismissed. His deputy, John Sherman, was serving as Acting Director. The post of Deputy Director for Science had been vacated by Bob Berliner. The Assistant Secretary for Health, Charles Edwards, was not particularly sympathetic with the goals of the NIH. He was a product of the Food and Drug Administration which is a regulatory agency, in contrast to the NIH which is primarily a research and research-support organization. It fell to his responsibility to select our new Director, and after a considerable interregnum he hit upon an unanticipated choice--Dr. Robert S. Stone. Stone had commenced his professional career as a pathologist at P & S. He had moved to the University of California, Los Angeles, and from there to the chair of pathology at the University of New Mexico. When the deanship at that school fell vacant he was selected as dean. When I first met him he was on leave of absence, assigned to the Sloan Institute of Management at MIT where he was both studying and teaching management procedures as these impinged upon biomedical sciences. Clearly this last item in his background was appealing to Dr. Edwards. It was his hope that by bringing Stone to the directorship of NIH he could effectively whip the scientists at NIH into line. When Bob Stone was first brought for his initial meeting with the institute directors of NIH, the mood was distinctly chilly. Only one of us--Ted Cooper, then Director of the National Heart and Lung Institute--knew Stone, and their earlier contacts at the University of New Mexico had not been friendly. We were, I think, appalled at the notion that a brisk wagger was being imported to guide the futures of our institutes. In the months that followed, an evaluation of Bob Stone changed a very great deal, and before his departure I fully appreciated him as a man of remarkable honesty, keen intelligence, great industry, and great dedication. He has suffered from a flaw in constitution which I can appreciate as I share this same defect. We both have encountered problems in our careers in sustaining good relations with our superiors. It is, I believe, a fact that most of us fall into one of two categories: either we get along fine with our superiors and are not held in high esteem by those who work under us, or we

have the best of relations with those below us in the hierarchy but have strained relations with those above. Bob Stone and I fall into the latter category.

It was Stone's responsibility to fill the position of Deputy Director for Science. After casting about, he and John Sherman approached me as to whether I would accept this job. I did so with some hesitation. By this time I was 65 years of age and my vision was deteriorating perceptibly. At my suggestion, they consulted with the Director of the National Eye Institute, Dr. Carl Kupfer, who had taken over supervision of my macular disease. Notwithstanding my visual defect, Stone made me a firm offer which after some consideration I accepted. On recommendation of Lee (Mrs. Robert) Berliner, Marney and I moved from our modest semi-detached home into the palatial Georgian house set apart for the Deputy Director for Science. This house provided a fine area for large-scale entertainaent on the main floor, and no less than seven bedrooms which during our occupancy, stood vacant most of the time. Only during Christmas family reunions and on the occasion of daughter Mary's wedding were all of these bedrooms occupied. There are two such fine private homes on the grounds of the NIH, and the other was occupied by Bob and Mary Stone. Together with Nancy Hawes, I moved into a sumptuous office in Building One. I brought with me from the staff of NIGMS Dr. Philip Chen, Jr., a man who has consistently exhibited great intelligence, enormous knowledge of the persons and regulations at NIH, great personal loyalty, and tremendous devotion to duty.

When I accepted the position of Deputy Director for Science, it was with the distinct understanding that John Sherman would continue as Deputy Director. John was held in high esteem and affection by all who had worked with him. In some way unknown to me, however, he had succeeded in arousing some hostility downtown, and his position at NIH was soon made so uncomfortable that almost tearfully he elected to leave for the vice presidency of the Association of American Medical Colleges. He continues to be a neighbor of NIH, to give good counsel, and to serve on the board of the Foundation for Advanced Education in the Sciences, Inc. Recently, I have served as executive secretary to the Alumni Association of NIH, of which John is the president.

The position of Deputy Director was soon filled by Ronald Lament-Havers, whom I had known for many years while he served in the extramural side of the Arthritis Institute. A genial and jovial man, he proved himself to be a good administrator, and thus in short order a new triumvirate--Stone, Lament-Havers,

and Stetten--replaced the earlier triumvirate of Marston, Sherman, and Berliner.

My relations with my new colleagues were easy and smooth. I found that Bob Stone was in substantial agreement with me on the importance of basic science support and of the investigator-initiated research project. He did make one feeble attempt to transmit to his staff some of the concepts of management which he had learned at MIT. We did listen to a few lectures by MIT faculty on goal-directed management, but the consensus of the institute directors and the top staff was that these principles had very little to do with us. To his credit, Bob Stone soon stopped trying to indoctrinate us with management strategy.

A striking characteristic of Building One that I encountered when I moved in was the almost complete absence of any scientific intercourse. There was endless discussion of matters of budget, politics, personnel policy, buildings, contracts, and of activities in the legislature and in the Office of Management and Budget, but virtually no discussion of research or of science. Indeed, only a few of my fellow inmates seemed to have retained much interest in such matters. Among these were Leon Jacobs, a parasitologist, who was at that time directing the contracting activities for NIH; Robert Gordon, a clinical investigator, who had become a special assistant to the Director; and my own staff of two junior associates-- Phil Chen and Bernie Talbot. In order to nourish our scientific curiosity, I established a weekly seminar in my office to which, in rotation, each scientific director was invited to bring two or more of his scientists. The instructions were very simple. For a period of two hours, from 10 to 12 on Friday morning, no administrative problems were to be discussed. Matters of salary, personnel, space, annual leave, and foreign travel were to be avoided. Discussion was to center about laboratory and clinical research activities, particularly those which were current. These seminars proved to be quite successful. They served as a liberal and continuing education for my immediate colleagues and me, and they provided to a sample of the scientists an opportunity to visit Building One and to speak about the things which interested them most. I was surprised to learn that many of the scientists had never been in the front office and seemed pleased to have been invited. These seminars have continued up to the present. Currently they are held in a room in Stone House, and in addition to my cronies from Building One the Fogarty visiting scholars are invited to attend. Over the years this

series has given me considerable insight into many different research programs proceeding at NIH. We have all been impressed by the uniformly high quality and the extraordinary diversity of research currently under way.

Among my responsibilities as Deputy Director for Science was the chairmanship of the semi-monthly meetings of the scientific directors of the several institutes. These were by tradition relatively free-wheeling meetings in which many topics of interest to the scientific directors had been and continue to be the most democratic events which occur in an otherwise hierarchical structure. Most meetings that take place at NIH are primarily designed to permit the chairman to share information with the participants. There is usually no agenda, votes are rarely if ever taken, and minutes are usually not kept. The scientific directors, however, preserved these parliamentary practices and enjoyed free discussions and arguments. A major and continuing function of this group has been to review promotion actions of scientists. This is an important process and is designed to preserve some equity in grade levels among the several institutes.

Undoubtedly the most time-consuming and most interesting activities that engaged me during my tenure in Building One stemmed from the development of recombinant DNA technology. I little knew what I was getting into when Bob Stone called me into his office one day in the fall of 1974 and asked me to assume chairmanship of a new committee which was to be called the "Recombinant DNA Molecule Program Advisory Committee" of the NIH. This committee was made up chiefly of outside scientists who had familiarity with one or more aspects of this problem, and was assembled in response to a request transmitted by my old friend, Phil Handler, President of the National Academy of Sciences, and contained in a letter signed by Paul Berg and a number of distinguished investigators urging this action. This letter, which had been published in Nature and in Science, was the consequence of an earlier concern expressed by Maxine Singer of NIH and Dieter Soll that there might be an inherent danger in the injudicious insertion of genetic information from one species into another. Two specific recommendations were that an international meeting be summoned to consider these problems and that a committee of the NIH be established to consider conditions under which it would or would not fund research in this area. The meeting was held in February 1975 at the Asilomar Conference Center in California, and accompanied by Leon Jacobs and Bill Gartland of NIGMS I attended this meeting.

It must be understood that there was not then nor has there developed since any evidence that the hazards which were considered have any reality. The discussions at Asilomar were designed to raise levels of anxiety and were eminently successful. Representatives of the press were present by invitation and they succeeded in spreading a wave of anxiety across the nation. Our committee held its first meeting in San Francisco on the day following the Asilomar conference. There was wide acceptance of the notion that guidelines should be generated to instruct scientists engaged in this type of research as to what they should and should not do, and these guidelines served as a model for the guidelines which were finally submitted to the Director, NIH, by my committee. All of this took time and much effort. A subcommittee, headed by Dr. David Hogness of Stanford, prepared a draft for subsequent discussion and this was the basis for a document tentatively adopted at a meeting held in July 1975 at Woods Hole, Massachusetts. When this document was distributed among those interested, we received a wave of angry correspondence. Most of these respondents felt that we had been far too lenient but others felt that we had been far too restrictive. A second draft was therefore prepared by a committee chaired by Elizabeth Kutter. In preparation for the next meeting, Bernard Talbot and his loyal secretary, Cathy James, prepared what I named the variorum edition, in which were given all the variant readings of the several sets of guidelines. This permitted the committee rapidly to vote upon each questionable matter, and so in La Jolla in December 1975 we finally came to a set of guidelines which seemed to satisfy all the members of the committee. It was a lengthy and complex document that we brought home to Bethesda.

By this time there had been serious political upheaval in Building One. Robert Stone had managed to engender hostility in the office of the Assistant Secretary for Health. This was apparently fueled in part by Ted Cooper, who had left his position as Director of the National Heart and Lung Institute to become Deputy Assistant Secretary for Health. Cooper and Stone had been colleagues in New Mexico and, as mentioned earlier, apparently were not overly fond of each other. At all odds, Bob was displaced and over the ensuing months Donald Fredrickson, also originally from the National Heart Institute but for the preceding year the President of the Institute of Medicine at the National Academy of Sciences, was named Director, NIH. When I reported the success of our activities at La Jolla to Don Fredrickson, he told me that he would now present these results to the Director's Advisory Committee, enhanced by

representatives of many public interest groups. I am told that when I heard this decision my only comment was, "Oh my God."

The press had done its work well, and the anxiety directed toward recombinant DNA research was acute. It was doubtless exalted by the popularity of Crichton's The Andromeda Strain, which had captured popular fantasy. The fear that the mad or irresponsible scientist might let loose upon the world a chimera that would engulf civilization was rampant. Fredrickson's decision to open this matter for public discussion had the effect of placing the microphone and the podium at the command of anxiety-ridden but frequently poorly informed persons. It is true that a handful of scientists shared in the persistent anxiety. These included Bob Sinsheimer, Berwyn Chargoff, and Nobel laureate George Wald. I had approached the problem cold at the time of the Asilomar meeting and had no firm convictions. In the beginning I found myself persuaded by whoever it was who had last spoken to me; but with the development of time, with increasing exposure to both sides of the argument, I had become convinced within the first year that the hazards were enormously overstated--if indeed they existed at all. I remember that on my flight to La Jolla in December of 1975, I shared airplane space with Maxine Singer. Two articles had recently appeared presenting diametrically opposing points of view--one by Bob Sinsheimer reemphasizing the hazards of this kind of research and the other by Josh Lederberg belittling these anxieties. I had been favorably impressed by Lederberg's presentation, whereas Maxine at that time still clung to the view espoused by Sinsheimer. We debated the matter warmly during the five-hour transcontinental flight. Prior to publication of the guidelines in the Federal Register, they were largely reworked in Don Fredrickson's office. The chief contributor to this revision was Joe Perpich, Associate Director for Program Planning and Evaluation, a physician trained in psychiatry and also a lawyer. His concern with the guidelines was almost entirely procedural, with repeated statements to the effect that what really mattered was the process whereby the final course of action was reached. I had the distinct impression that for Joe the process was more important than the eventual action, an attitude with which I could generate little sympathy. What I observed, however, was a gradual erosion of the notion of "guidelines" to be replaced by the notion of "regulations." The original assignment had been clearly to generate guidelines, and this I construed to mean advice given by the committee to the scientist which he would do well to take quite seriously. Regulations, however, were quite

another matter. A violation of regulations is almost the same as a violation of law. We had carefully put many of our words in the form of an injunction: "The scientist should" or "The investigator ought to." These were in almost every instance replaced by the words: "The scientist shall" or "The investigator must." Clearly, if our guidelines were to become regulations, then provisions must be written to indicate how these would be enforced and how the violator would be punished. These were not discussed in the original guidelines nor have I ever felt that they constituted an appropriate part of our committee's action. Nonetheless, it was so ordained in Fredrickson's office and it was in this form that publication occurred. Almost at once it was apparent that there were many defects in the guidelines. This became obvious when the committee started trying to adapt applications by scientists to the rules that had been set down. Many applications simply did not fit and some inquiries led to preposterous conclusions. Therefore, almost as soon as the guidelines were published we set to work to revise them. As a very minimum, it seemed to me essential that the Byzantine structure of committee procedures and reports had to be simplified lest an undue fraction of America's best bioscience talent be captured in procedure when it should be devoted to research. I therefore urged my committee, as persuasively as I was able, to simplify procedures and abbreviate the guidelines. It is, however, very difficult for a committee ever to be brief. As a sample of one of my arguments, I should like to include here a paper which I had published in Nature,* trying to point out the fallacies of the course upon which we had proceeded.

A Parable on Recombination

Scientists and nonscientists are currently polarised in their assessments of the hazards attached to the creation and handling of recombinant DNA molecules. Whereas the hazards are of unknown dimensions, the anxieties are clearly great; but the magnitude of the anxiety is a very imperfect measure of the magnitude of the hazard. Among the diverse views we are seeking an area of possible agreement or, better yet, an area of truth.

Truth is sometimes found in unexpected places. It may be recalled _ that Jonathan Swift, famed satirist and author of Gulliver's Travels, while serving as Dean of St. Patrick's in Dublin, considered the

* Nature, 266, (7 April 1977), p. 488.

disastrous problem of the famine among the Irish peasants which was aggravated by the high birth rate and the abundance of children. He analysed the problem in 1729 in an essay entitled 'Modest Proposal for Preventing the Children of Poor People from being a Burden to their Parents or the Country,' in which, with all pretense of reasonableness, he concluded that the entire problem could be solved if the people of Ireland ate the children. In view of the evident success of Swift's satire, I am taking the liberty of presenting here a parable which I call 'Genetic Recombination--A Modest Proposal'.

After all, recombinant DNA technology is a special case of a far more general phenomenon--that of genetic recombination itself, where genetic material from two sources is repeatedly combined within a single cell. It happens when an oncogenic virus invades a mammalian cell, or when a bacteriophage invades a bacterium. It happens when two bacteria enter into conjugation and transfer plasmid DNA from one to another. In the laboratory it can be achieved through the hybridisation of eukaryote cells from widely differing species, and it is of course the very basis of sexual reproduction.

A form of this kind of experimentation which has been popular for a very long time indeed results in the fertilisation of the human ovum. I refer to this exercise as an experiment, because it always is experimental in that the outcome is not known a priori. At this time we can not even foretell the sex of the offspring, much less any of the details of its anatomy or character. Yet the experiment, whereas it provides great possibilities of useful and benevolent results, does have a real hazard. Textbooks of obstetrics contain many engrossing photographs of anatomical monsters which have resulted from this process, but it seems to me that the very worst monsters, the behavioural ones, are not included. These may be divided into two classes--the societal monsters such as gangsters, typified by Al Capone, and the international monsters, exemplified by Adolf Hitler.

Clearly, some of these monsters possess a survival advantage over the rest of us. One has merely to note the direction in which the machine gun which the gangster carries is pointed to ascertain which party is in the better position to survive the encounter. Of particular interest is the experiment conducted nearly ninety years ago by the parents of Adolf Hitler. The maternal ovum may be construed in this case as the host, while the paternal sperm clearly was the vector, bearing as it did a charge of DNA which was foreign to the host. The conceptus which resulted was carefully cloned under reasonably sterile and controlled conditions, and there arose an individual who became, directly or indirectly, responsible for the premature deaths of 4×10^7 human beings in the course of about eight years. This mortality is certainly large, even in the parlance of the epidemiologist.

When scientists first began to appreciate the danger attached to the fertilisation of human ova, they directed attention to the matter and called for an immediate moratorium. Since the hazard seemed to be of enormous proportions, the federal government soon became

involved; and by and by, a Presidential commission was established to consider the problem and to determine its best resolution. With the moratorium still in effect, one alternative solution proposed was to sterilise all adults, male and female. It was forecast that this procedure would probably work, but it would be quite costly. For this reason, the General Accounting Office, which has the responsibility of surveying costly federal projects, gave its attention to the matter and pointed out that sterilising of either the male or the female population would probably achieve the same desired effect at half the cost. To decide whether to sterilise all males or all females, a special panel of the Equal Employment Opportunity Commission was convened which, with Solomonic wisdom, recommended that since there were approximately equal numbers of males and females in the population at risk, it would appear appropriate to sterilise half of the males and half of the females.

A small experiment was conducted on normal volunteers to test the effectiveness of this procedure, and it was found, for reasons which are still unclear, that this procedure would not yield the desired result. After considerable deliberation, the commission recommended that experiments in human impregnation might proceed with caution in certain designated centres, provided steps were taken to preclude pollution of the environment. It was determined that experiments could be conducted under 24 physical containment with all the manipulations to be carried out in class III safety cabinets which, in the usual fashion, would have their entry and exit ports protected either by autoclaves or by incinerators. Only in this way could the public be assured that no monsters would escape to pollute the environment and damage the ecology. The econiche which we so comfortably occupy would not be threatened by another generation which predictably would perform less nobly than we had done.

While the above note attracted some favorable attention, it did not, I think, convert many of the now frightened members of the general public. I found to my dismay that while most of the members of my committee were in reasonable agreement that the basis for the original wave of anxiety was rapidly disappearing, a view receiving support from experimental results of Hartin and Rowe, the committee elected to assume a political rather than scientific role and felt that it was necessary in some degree to appease the opposition. I felt, on the contrary, that if indeed there was no scientific basis for the anxiety, our committee, which was after all a scientists' committee, should so state publicly and move toward the elimination of all unnecessary guidelines and regulations. Frustrated by my inability to sell this case either to Don Fredrickson or to the members of my committee, I determined to resign my chairmanship. My resignation message was carefully considered and I include it herewith.

Valedictory by the Chairman of the NIH Recombinant
DNA Molecule Program Advisory Committee*

I am taking a Chairman's prerogative to invade the printed agenda. I should like to share with you the reasons why I have felt impelled to resign my chairmanship of this Committee. Shortly after our last meeting of November 1977, I asked the Director, NIH, to accept my resignation and find a replacement for this chairmanship. He asked me to assist in the selection of a new Chairman and I have provided to him the names of candidates from which he is soon to make a choice. I am certain that you will be pleased with the name of my successor, and that the Committee will give the new Chairman the same devotion and industry which it has given to me.

There were, of course, personal reasons for my resignation. I am four years older than I was when I was first appointed, I fatigue more easily, and, as you are all aware, my visual acuity has continued to decrease until I am able to read only a very small fraction of the large amount of paper which passes over my desk in relation to this function. In addition, I have had a growing unhappiness with some of the directions which the recombinant DNA program has taken over the past four years. From my conversations with members of the Committee, I believe that this unhappiness is shared by some of you, and this may be a good opportunity to verbalize this discontent.

Prior to the Asilomar meeting of February 1975, I had had only modest contact with nucleic acids and with genetics. I had worked in the laboratory with lipids, polysaccharides, and proteins, but had never handled any nucleic acids. I had never worked on a genetic problem, and had certainly never engaged in microbiological research. Except for some briefing which I secured from members of the intramural NIH family, I came to Asilomar cold.

It has taken me several years to analyze and unscramble the experience of the Asilomar meeting. I now understand it more fully than I did at the time. It had many elements of a religious revival meeting. I heard several colleagues declaim against sin, I heard others admit to having sinned, and there was a general feeling that we should all go forth and sin no more. The imagery which was presented was surely vivid, but the data were scanty. I recall one scientist presenting information on the difficulty of colonizing the intestinal tract with Escherichia coli K-12, but his presentation was given little attention. We were all, in effect, led down to the river to be baptized and we all went willingly. I, for one, left the meeting enthralled. I had never been to a scientific meeting which had so excited me. On my return to Bethesda, I was asked to summarize the events at Asilomar before a meeting of the generally staid NIH Institute Directors and I believe I was able to transfer to them some of my excitement. Over the succeeding months, the recombinant

* Gene 3 (1978), 265-268

DNA Molecule Program Advisory Committee met and, by July 1975, it drafted a set of guidelines at Woods Hole, Massachusetts, which I at the time thought to be reasonably satisfactory. They did not conform to my prior notion of guidelines exactly, since they bordered on the encyclopedic. Nonetheless, I felt that we had successfully compromised most of the burning issues over which the Committee was initially strongly divided. When these guidelines were distributed, however, they elicited vigorous and often emotional responses, and among these responses there was one which I recall vividly. It charged our Committee with having violated the "spirit of Asilomar." At the time this expression did not catch my attention, but on consideration I was struck by the fact that despite the many, many meetings which I had attended at Atlantic City, I had never heard a reference to the "spirit of Atlantic City." This charge, in fact, pinpointed for me the notion that the experience at Asilomar was essentially a spiritual one rather than an intellectual one. It was, in the usual sense, not a scientific meeting at all. Whatever its purpose may have been in the minds of its initiators, a result was to fire the imagination, first, of the newspaper correspondents who were abundantly represented, and then of a substantial segment of the newspaper-reading public.

By December 1975, our Committee, meeting at La Jolla, again assembled a set of guidelines. Whereas up to that time I had insufficient confidence in my own judgment to hold a firm opinion on this issue, and found myself swayed by the views most recently presented, it was about the time of the La Jolla meeting that I began to wonder whether, indeed, any of the postulated hazards of recombinant DNA molecule technology were likely to materialize.

The La Jolla guidelines served as the basis for a discussion at a meeting of the NIH Director's Advisory Committee early in 1976, and this, in turn, was followed in July by the publication of the official NIH guidelines. In this last transformation, something happened which I found disturbing.

The mission of NIH is, I believe, very simply stated. It is to conduct and to support the very best biomedical research that it can find to conduct and support. Similarly, the mission of our Committee and of the guidelines which it drafted was to provide assurance that research in the area of recombinant DNA molecules would be conducted in such a fashion as not to jeopardize the laboratory, the community, or the environment. Both missions, it should be noted, are stated positively. It is the purpose both of NIH and of this Committee to encourage, to promote--not to forbid or to impede. The legal profession represented at the Director's Advisory Committee meeting was critical of the concept of guidelines, which in my judgment are designed to provide guidance to the investigator and to those who review his proposal. We were informed that what was needed was regulation, not guidance. This was exemplified by the recommendation that our instruction, written largely in the subjunctive mood (the investigator should . . .), be replaced by the more peremptory language of regulations (the investigator shall . . .). I recall arguing against such change in vain.

My reasons were very simple. It is my interpretation of the history of science and indeed of all culture that regulation is antithetical to creativity, and creativity is the most important component of scientific advance. From this, it follows that the best regulation for the flowering of science is the least regulation--that is, the least regulation compatible with the needs of society. Furthermore, I feared and my fears were, I think, justified that regulation might lead to legislation with a specification of sanctions, i.e., punishment, for those who were in violation of the regulations. Whereas the so-called regulatory agencies of Government must from time to time adopt a punitive posture, this is, I believe, a poor posture for a research agency such as the National Institutes of Health.

Against what hazards were we proposing to draft regulations? With the passage of time, the hazards that had been pictured at Asilomar seemed to recede. Whereas a great number of positive and useful scientific results are being published based upon the technology of recombinant DNA molecules, to the best of my knowledge no adverse results have been noted. Indeed, I believe that there is at this time not one iota of acceptable evidence, i.e., data publishable in a scientific journal, to indicate that the recombinant DNA molecule technology has ever enhanced the pathogenicity or the toxigenicity of any microorganism. This, of course, does not mean that it never will do so, but it does cause one to wonder whether all of the present fuss is truly justified. It places the hazards in this area in the same category as those in many other areas for which we have no positive evidence. To clarify this point, let me offer you an analogy. Ever since the Middle Ages, it has been suspected that the ghosts of those who died by suicide are more menacing than ghosts in general. This anxiety, once implanted in the minds of the people, led to some interesting containment practices. The bodies of victims of suicide were excluded from traditional burial places, lest their ghosts pollute or otherwise disturb the more peaceful ghosts of those who died of natural causes. They were doomed to be buried in the crossroads, and in order to ensure that the ghosts not escape from the tomb, a stake was driven through the body of the victim into the underlying soil, thus pinning the ghost into its grave. This containment practice continued for many centuries and was ultimately abandoned only in the 18th century. Experience since that time has justified the conclusion--that the hazard which had earlier been postulated was either of very small magnitude or possibly nonexistent. We may yet prove to be wrong about the safety of unpinning the ghosts of suicide victims, but I should be surprised if this were so.

How long do we wait in the absence of any positive evidence before we decide that the hazards in a particular area of research are at a socially acceptable level? To this question I have no specific answer. Soon we may come to the conclusion that the manipulations of recombinant DNA technology do not of themselves add significantly to the dangers inherent in the conduct of microbiological research. Then we can replace our complex and, I repeat, encyclopedic guidelines by a very simple statement. This might take the following form: "The conditions of containment appropriate for any recombinant

DNA experiment are those which are dictated by the most virulent or dangerous organism entering into that experiment." Is anything more really required?

I hope that none of you will construe any of my critical remarks as being personally directed. They are not. I have thoroughly enjoyed and been stimulated by my contacts with the many members of the Committee. I hope that I have established enduring friendships with many of you, and I shall certainly follow your further deliberations with great interest and concern. I should like particularly to express my appreciation to the several members of the NIH staff who have worked so hard and so loyally to keep this project afloat: Dr. Leon Jacobs, who from the beginning has served as Co-Chairman of this Committee; Dr. Bernard Talbot, who has worked enormously hard and valiantly; Dr. William Gartland, Director of the Office of Recombinant DNA Activities, and his small but energetic staff-- Dr. Kamely and Dr. Goldberg. Then, there is Ms. Betty Butler, who not only made certain that all the paper flowed in the right directions but also nursed us through our several tortured meetings. To work with all of these people has been a very rewarding experience.

I wish you well in your future meetings.

At my recommendation, Fredrickson appointed Jane Setlow of Brookhaven National Laboratories to succeed me, and she in turn was succeeded by former Congressman Thornton. I am happy that the committee has finally taken major steps to reduce the experiments over which guidelines are still imposed, and I look forward over the years ahead to the gradual adoption of the one-sentence guideline included in my Valedictory comments, or something equivalent to it. In retrospect, the entire episode now appears to me to have been a somewhat hysterical outburst led by a group of imaginative scientists who were in some degree fired by contemporary science fiction, and who confused, as we often do confuse, anxiety with hazard. Of real hazard there never was any indication. This tendency to confuse hazard with anxiety is not novel. It is quite clear from many examples that the level of anxiety is a very poor measure of the real danger, that man tends to be most frightened by spectres of no real substance and is inclined to relegate real and present dangers into a secondary position. Thus, sea monsters and invaders from outer space are far more awe-inspiring than truly damaging threats such as handguns, automobiles, and above all cigarettes. To secure effective regulation of the latter has proved essentially impossible. I should guess it would be very easy to get a bill through Congress placing nets around our shores; to exclude sharks, or imposing the

severest penalties on all occupants of unidentified flying objects who land in the United States.

There are, of course, many current developments in the industrial applications of recombinant DNA technology. One of the more interesting has recently been announced in the newspaper--namely, the preparation of a very pure foot-and-mouth disease antigen prepared by the cloning of the viral DNA. This experiment was one of the absolutely forbidden types of experiments in the original guidelines, yet apparently it has been conducted without any adverse effects. Among the anticipated benefits is the possibility of eradicating foot-and-mouth disease in Argentina, making Argentine beef again available to the United States market. Should this happen, we can anticipate a fall in the price of beef and beef products at the store, a wholly unanticipated dividend of the cutting and splicing of genes in the molecular biology laboratory.

During my years at NIH I have served under many Directors. These include Sebrell, Shannon, Marston, Stone, Fredrickson, and Wyngaarden, and in addition Acting Directors Sherman, Lamont-Havers, and Malone. Of these, the one who made the most profound contributions to NIH in my opinion was Jim Shannon. In fact, the present NIH is very largely the culmination of his dreams and actions. This view of mine is, I believe, shared by many others, and among these is James Dickson. Jim, whom I came to know well during my stay at NIGMS, has a most unusual background. He was trained as a thoracic surgeon, a specialty which he practiced in the United States Army in Korea. It was during this term of service that he became the model for one of the chief characters in the movie and television serial M*A*S*H. Subsequently abandoning the practice of surgery, probably because of developing rheumatoid disease, he took some training in engineering and came to NIGMS to direct its biomedical engineering program. He is certainly of Irish ancestry and hails from the neighborhood of Boston where he has associated with several members of the Kennedy family. He has a deep and lively interest in practical politics, and on many occasions I have dropped in at his office in order to secure his insight into recent political problems. He is a man of wit and of political savvy. It was during one of these conversations that we jointly came to the conclusion that something should be done to memorialize Jim Shannon. Shannon had become director of NIH when Henry Sebrell left and it was during these years that the institutes had their greatest growth. He was a strong and discriminating leader, always insisting upon the highest quality of research,

and he placed his personal imprint upon the National Institutes of Health. Our initial thought was to have his name given to the Clinical Center, the vast red brick building which houses all of intramural NIH's clinical activities as well as many of its laboratories. This, it turned out, was extremely difficult to do. Federal buildings are only occasionally named after living persons and then only by act of Congress. In point of fact, subsequent to our initial discussions, the Clinical Center was renamed after Senator Magnuson, Chairman of the Senate Appropriations Subcommittee for HEW and a sponsor of much of my enabling legislation. Therefore, in quest of some other way of showing our appreciation to Jim Shannon, I determined to provide for NIH a bronze bust of our favorite director. Clearly this could not be purchased with appropriated funds. I therefore contacted a number of directors of pharmaceutical laboratories who had reason to appreciate both Shannon and the NIH. The result was the prompt assembly of sufficient private dollars to permit us to engage the services of Elaine Pear Cohen, the wife of fellow biologist Seymour Cohen. Elaine has achieved considerable reputation as a portrait sculptor, and it was my privilege to bring her together with her new subject. They apparently got along famously, and after several weeks a fine bust in plaster was completed. This was then delivered to the foundry, and sometime thereafter the bronze figure was delivered to NIH. She had a pleasant unveiling ceremony and the bust has since stood on a pedestal in the lobby of Building One. It had seen my hope that the bust would move to the lobby of the expanded Clinical Center upon completion of the Ambulatory Care Research Facility, but since Building One was renamed the James A. Shannon Building on January 18, 1983, it would seem appropriate for the bust to remain where it is.

It was during my years as Deputy Director for Science that my vision finally failed. By the end of my stay in that office I was no longer able to read even the largest type. I became increasingly dependent upon various audio services, particularly upon the willingness of Nancy Hawes and Phil Chen to read material to me. The job, however, was one which required my signature on many documents, and in the Federal Government to sign documents which you have not read carefully is a hazardous procedure. Therefore, in September of 1978, I asked Don Fredrickson to search out my replacement. For nearly a year nothing seemed to happen and I became increasingly discontented with my role. The prospect of going blind depressed me to such an extent that I finally, at the age of 70, did something which I had never done before. I consulted a psychiatrist. In

fact, I called up Dr. Robert Cohen, a colleague of many years' standing and the chief of clinics in the National Institute of Mental Health. I had used Dr. Cohen's advice and services many times during my years at NIH whenever one of the scientists for whom I was responsible or the spouse of a scientist deviated from sanity sufficiently to warrant such a consultation. Bob had always come through with flying colors, giving remarkably sensible assistance. In the case of my own consultation, he listened carefully for about one hour while I recited all my woes, most of which related to the fact that I no longer could see. In the end he smiled benignly upon me and gave his verdict: "You know, Hans, you are depressed, but you are no more depressed than you ought to be." This diagnosis cheered me enormously and has assisted me in coping with the developing handicap.

Chapter XV

"THIS DARK WORLD AND WIDE"

The master bedroom of our home in the suburbs of New Brunswick, New Jersey, had a picture window which looked out over the Delaware and Raritan Canal. It was one morning about 15 years ago while still lying in bed and inspecting our view that I first noticed that; whereas the horizontal lines of the window frames were perfectly straight, as they should be, each vertical line contained a previously unnoticed bulge. While I watched, these bulges moved downward toward the floor. Here was a new and puzzling illusion that I could not understand, and so I called my ophthalmologist, Dr. William Rubin of New Brunswick, and described the problem to him. He at once appeared to sense that this was something important and told me to come to his office as soon as possible. After studying my retina ophthalmoscopically, he concluded that I apparently had macular degeneration. Recognizing the sinister implications of this diagnosis, I called an old friend, Dr. Charles Perera, who was the older brother of a schoolmate of mine at Horace Mann--now a senior professor of ophthalmology at the College of Physicians and Surgeons, Columbia University. After examining my eyes with an array of optical instruments, he unhesitatingly confirmed the diagnosis and told me that this was a progressive disease for which there was no useful therapy. Over the ensuing years, very insidiously at first and then somewhat more dramatically, my vision deteriorated. I first lost fine discrimination, then gradually I became unable to locate or to identify gross structures. Later I lost most of my color perception. I stopped driving a car about 10 years ago. About six years ago I became legally blind, and four years ago I lost all ability to read regardless of magnification.

In 1971, having returned to Bethesda, I placed myself in the hands of Dr. Carl Kupfer, Director of the National Eye Institute, who had a particular interest in retinal disease. On his recommendation I was seen in consultation by Professor Edward Maumane, chairman of the Department of Ophthalmology of the Johns Hopkins Medical School. Although the macular lesions were apparently not typical of those seen in traditional macular degeneration, and although my loss of visual acuity seemed to exceed that anticipated from the appearance of my retinas, the fundamental diagnosis was not questioned. About five years

ago, developing cataracts suggested that some relief might be secured by appropriate surgery. In anticipation of this, I was again studied by the doctors at Johns Hopkins, and for the first time I heard that I might, in addition, be suffering from "soft glaucoma." This name, which seems paradoxical, implies the existence of occasional periods of elevated intraocular pressure. To explore this possibility, I was hospitalized for 24 hours, during which period intraocular pressure readings were taken at frequent intervals. The values secured were not incompatible with the diagnosis. I was therefore advised, belatedly, to instill eyedrops into my eyes at frequent intervals. The cataract was removed about two years ago from my left eye, which had the better preserved retina. Some slight improvement in vision did result from the surgery, but my peripheral vision unexpectedly continues to deteriorate.

I was not emotionally prepared to be disabled, having always enjoyed moderately good health. I did have a myocardial infarct in 1965 but the hardest part of this was the severe hospital regimen to which I was subjected. This was still in the period when the dicta of Paul Dudley White were strictly observed and I was kept flat on my back for six weeks. From the infarct itself I suffered no significant adverse consequences but it took me some time to recover from the bed rest. My other illnesses have all been minor. But for the last four or more years, blindness has dominated my every waking moment and has determined my way of life.

At Woods Hole I had come to know Daniel "Spike" Carlson, a biophysicist, who was connected with the Johns Hopkins Department of Biology. He had suffered severe visual impairment rather similar to my own, and it was from him that I learned about the Talking Books Program, which is administered by the Library of Congress National Library Service for the Blind and Physically Handicapped. Certain designated community libraries, including the one situated in Rockville, Maryland, not far from Bethesda, participate in this program, which provides to its members a special cassette player that operates at the slow speed of 15/16 inch per second, and a special record player that operates at 8 rpm. What is most important, the library also provides at no cost a very wide selection of books that have been recorded on tapes or records numbering approximately 350,000 items. Furthermore, new items are continuously being added and subscribers receive bimonthly a bulletin of these new items from which they may make requests. Sooner or later these selected books arrive and may be enjoyed at home. They are then mailed back to the library at no postal charge. The

Service is altogether remarkable and has provided for me the difference between sanity and madness. I am never without a stock of listening material at home. I find the cassette tape format far more convenient than the phonograph and have the tape player equipped with a pair of earphones at my bedside. A fringe benefit is that listening to tapes in the dark is a remarkably sedative experience, a powerful cure for insomnia. Contrary to the hopes expressed by some educators, the material delivered to the ears while one is asleep leaves no residual impact whatsoever.

In addition to books, I also listen to several magazines. Newsweek arrives every week on three disposable phonograph records. It takes approximately six hours to listen to the entire magazine, which is more time than one would normally dedicate to Newsweek. Skimming, however, proves to be rather unsatisfactory in the phonograph format. It is more easily performed in the cassette tape format. I am therefore delighted that Scientific American and Medical World News come on cassette tapes, tone coded. This means that every article is preceded by an audible beep and permits the listener rapidly to select the article which he wishes to hear. These three journals, whereas they are far less than I used to glance at in earlier times, approximately cover my regular magazine listening.

The entire process of listening to the literature in this way works admirably. Occasionally a tape becomes tangled but this is unusual. Particularly gratifying is the quality of the voices of the readers. The enunciation is clear, the pronunciation is generally precise, and in many of the books the readers enter into the drama of the plot and do fine theatrical jobs. The world of the blind is deeply obligated to the many men and women who give of their time to read books and journals onto records and tapes, and to Mr. Cylke who directs the Talking Books Program.

A second piece of useful guidance which I secured from "Spike" Carlson directed me to Visualtek. This instrument, manufactured in California, comprises a TV monitor, a TV camera, a zoom lens, and suitable illumination equipment. It is so arranged that a book or other material can be placed under the lens, and its image, enormously magnified, appears on the TV screen. A switch permits you to select black letters on white background or white letters on black background. This instrument permits someone with diminishing acuity to continue reading long after the usual optical magnifiers have lost their usefulness. I kept this instrument in my office and used it fairly frequently

until recently, when I found that even with the great magnification provided I could no longer profitably use the machine. It is an instrument of great potential value, however, for many persons.

It was radio advertising that first called my attention to the Washington Ear. This is a local program that provides, at no cost to the subscriber, a small radio receiver pretuned to a single frequency not included in the standard broadcast bands. Every morning, starting at 7 o'clock, volunteers read the Washington Post covering all of its principal features. Since we Washingtonians hold the Post in very high esteem, and since it is now the only newspaper published in the Capital, awareness of its content is a sine qua non for survival. The Washington Ear publishes its schedule monthly. It includes two complete readings of the Washington Post each day, interspersed with other materials that may be of interest to its listening audience. I must admit that I have not listened to it with any regularity, since Marney makes it a practice to read the headlines, the editorials, and the op-ed page to me over breakfast, and since substantial blocks of time must be set apart to take advantage of the Washington Ear program. Were I fully retired I imagine that I might well make listening to the Washington Ear a regular practice.

In my office I have surrounded myself with a number of useful devices. The portable, handheld version of my dictating machine I now keep constantly on my desk and use it as others might use a scratch pad. Any bits of information which I wish to record and expect to have to recall--such as names of persons, telephone numbers and the like--I simply speak into my dictating machine for future reference. I have almost totally stopped trying to write since it usually ends in a miserable failure. My only writing today is signing my name to checks and occasional legal documents. My signature, I am told, is changing significantly. Another device which has proved useful is a push button panel attached to the telephone circuit that permits me to dial any one of 32 predetermined phone numbers by simply pushing one button. My secretary, Nancy Yellin, has put into the memory of this device the phone numbers that I call most frequently. I have found that I can easily dial using a push button or touch tone instrument. The traditional old-fashioned telephone dial is far more time consuming to use and I am prone to make errors.

The most sophisticated electronic device that I have is the Kurzweil Reading Machine. This instrument, designed and built by a group of MIT-trained engineers in Cambridge, Massachusetts, scans either the printed or the typewritten

page and recognizes and stores approximately 300 successive letters or numbers. Then, applying information about pronunciation of English words stored in its memory, it synthesizes these letters into sounds which come out of a loud speaker and which approximate spoken English. The synthetic voice is initially quite incomprehensible, but as one listens, one comes to understand it much as one learns to understand a dialect. Marney, who listens to it only occasionally, insists that it sounds like a foreign postdoctoral fellow giving a seminar during his first two weeks in this country. I find that now, after more than one year of usage, I can understand much of what it says on first reading. An array of push buttons permits the operator to go back and repeat words or lines which were not understood, and also, if a word is totally incomprehensible, the machine can be instructed to "spell it out." With fairly intense concentration and considerable repetition, usually the reader can master the material under study. The process, however, is tiresome and tiring. Then there are certain complications which the machine cannot master. For instance, if there is in the course of the text a figure, a table, or a photograph, the machine endeavors to recognize letters and to synthesize these into words. The result is gibberish. Also, if there is an abrupt change in typeface, as when one or more words are printed in italics, the machine usually is baffled. It sees these sloping lines of type which it apparently identifies with "1" or "7" and all at once it will say "////7777." No amount of fiddling with the buttons makes the message comprehensible. Furthermore, whereas the scansion works well for the normally printed page, if the page is multi-columnar in format, as is common in scientific texts and journals, the performance of the machine is inconstant. According to the instructions, it should be possible to tell the machine to first read column 1 and then column 2, etc. However, in practice I have found that the machine often will jump across from one column to the next; and whereas the words that result are comprehensible, the text is meaningless. All in all I have found the Kurzweil a very interesting development in computer science and electronics. It has, I believe, great promise and certainly provides for the totally blind individual access to printed or typewritten words. It still has many limitations on its potential usefulness. However, I have little doubt but that over the years ahead it will become more proficient. Already one can, by replacing the program which is in the form of a cassette of magnetic tape, transform the instrument into a calculator.

I first heard of the Kurzweil Reading Machine from my son, who was living at

that time with a group of MIT students in Cambridge, one of whom was working with the Kurzweil Company. The machine was exhibited in the Department of Health, Education, and Welfare and I went to inspect it. The National Institutes of Health has a program whereby unusual pieces of equipment may be purchased by its Division of Research Services and subsequently leased to one or another laboratory. I was sufficiently impressed by the Kurzweil Reading Machine to recommend its purchase, and some months later I had the instrument set up in my office. I soon mastered its operation, which was relatively simple, and have spent many hours listening to its performance.

There is, in fact, no perfect replacement for the live human voice. In Bethesda, both Marney and Nancy Yellin spend a good deal of time reading to me. During summers at Woods Hole, I have been able to hire young graduate students who are happy, for a modest fee, to read to me each day. Such an arrangement provides maximum flexibility and comprehensibility.

What is generally recognized is that as vision deteriorates one loses not only orientation in space but orientation in time. This happens when the victim is no longer able to read the clock on the wall or the watch on his wrist. I have derived enormous satisfaction from the recently marketed talking timepieces, both in the clock and in the wristwatch formats, and I am never far away from my talking watch. In addition to announcing the time, whenever I push the appropriate button it also has a charming alarm system which plays the familiar Boccherini Minuet.

I am presently 74 years of age and probably would, in the normal course of events, have retired by this time. Marney and I had discussed many possible activities which would engage our time after retirement. For myself, my most important and time-consuming hobby of recent years was working in wood. This included cabinetmaking and especially wood turning. I spent many happy hours at my lathe making bowls, platters, and boxes. I have done some furniture construction, some cabinet work, and have even tried my hand at inlay. Therefore, when we expanded our Woods Hole house, we built a large carpentry shop in the basement and I carefully assembled both hand and power tools. Now this activity is denied to me. I find it difficult to locate my hand tools. I am totally unable to read the rulers and other measuring instruments, and I have learned from experience to shun power tools. Marney and I had expected to travel widely during our retirement but travel entails sightseeing. The reader's attention is particularly directed to that word. Travel of that sort

is a distinctly limited source of pleasure for the visually handicapped. In addition, the activities of finding one's way through a crowded airport and of getting into and out of airplanes and other unfamiliar vehicles become very troublesome. We have given up going to the movies but we still go to theatre where Marney, sitting next to me, whispers in my ear from time to time the action and activity, which is helpful to me but seems occasionally to be disturbing to our neighbors. The Arena Theatre of Washington has recently introduced a program of providing to its blind clients over radio circuitry a running description of what happens on stage. I listen with one ear to the words coming from those on stage and with the other ear to the broadcast description of the action. The input is sometimes confusing but does add to the enjoyment of the visually handicapped persons in the audience. Other than the news, I listen infrequently to television, since I am unable to see any detail of the video image.

There is a whole large field of mobility training and devices with which I have had no direct contact. Whereas I can find my way easily about my home or my office, I rarely invade other areas unguided. If I take our dog out for a walk, I have found that I sometimes rapidly get lost. I therefore rely heavily on relatives and friends for guidance. Most of the time I am holding onto Marney's elbow, and she has become very expert in seeing that I avoid encounters with overhanging branches, garbage pails, lamp posts, and other obstructions. She calls my attention to curbs and other irregularities under foot and I have learned to heed her signals. Together each day we walk our dog, Daisy, a foundling that turned out to be a Tibetan terrier. Whereas I own a cane, I have never taken instruction in its use and probably for this reason I do not use it.

Many ordinary chores become complex and difficult as one loses vision. Dressing and undressing, selecting appropriate combinations of shirt, necktie, and suit, even making certain that the two shoes that one puts on constitute a matching pair--these are all problems to be solved. As one becomes blind, table manners certainly deteriorate. There is a tendency to knock the coffee cup or the glass off the table. There is often difficulty in finding the butter which one proposes to spread on the bread, and the carving of a chicken is very difficult, time consuming, and often ends in spillage. The temptation to pick the food up in one's fingers becomes almost irresistible, and one comes to depend upon one's neighbor for such activities as pouring-cream into the

coffee. To feed oneself at the typical Washington standup or buffet supper becomes essentially impossible, and I therefore decline such invitations unless Marney is also invited.

All in all, the prospect of retirement is far less attractive to me than it was a number of years ago. In my position as Senior Scientific Advisor to the National Institutes of Health, I continue to conduct the seminar series to which intramural scientists are invited to present their findings for the benefit of senior staff and of the Fogarty visiting scholars. I have initiated the assembly of a history of intramural science at NIH and am now securing contributions to this volume from distinguished members of the staff. These I review, criticize, and edit. I have initiated the collection of historic pieces of scientific equipment with the view of establishing a permanent exhibition in the Clinical Center of NIH for the enlightenment of future generations of biomedical scientists. Also, I am available at all times for consultations by all and sundry. My work here is for me far more engrossing than anything I could be doing in retirement.

My greatest pleasure comes from conversation with friends and colleagues who come to visit with me. Whereas large gatherings can prove confusing to a blind person who has difficulty in identifying the source of each voice, small groups of two to four are easily managed. The sense of hearing undoubtedly becomes more acute. The memory becomes more retentive.

Our oldest daughter, Gail, together with her husband, Peter, and their two children, Beth and Alex, live in Baltimore, and the frequent visits that we pay to them or they to us have become extremely important to me. A special relationship has developed between me and my grandson Alex who, at the age of four, came to the conclusion that it was a good idea to hold Grampa's hand when he walked around the house or up and down stairs. It is a heartwarming experience to have your small grandson act as your guide.

Many of my friends have suggested that they might read to me to me from time to time, and indeed several have done so. Most remarkable in this group is William Carroll, a chemist, now retired from the National Institute of Arthritis and Metabolic Diseases and serving as a teacher of science in the public school system of the District of Columbia. We had known Bill and Bunny for many years and spent a month with them in Boulder, Colorado, in 1958 as participants in a meeting on physical biology. Our contacts had not been particularly close, however, until one day as my vision was deteriorating Bill

suggested that he come to my home on a regular basis and that together we read books in the area of the philosophy of science. We started out with Godel, Escher, Bach by Douglas Hofstadter, and whereas we never finished this remarkably obscure volume, we did engage in stimulating conversation. We have since turned to Disturbing the Universe by Freeman Dyson, which Bill reads to me one or two evenings each week. It is an act of friendship and understanding of which I am deeply appreciative. The fact is that no mechanical device--whether tape, record player, or radio--replaces the voice and the intelligence of a sympathetic human being.

Over the years I have been puzzled by the fact that none of the several aids to my way of life that I have discovered was brought to my attention by any of the ophthalmologists whom I consulted. It seems to me that the student of diseases of the eye should be particularly well equipped to advise the visually handicapped on his sources of satisfaction and gratification, yet no such advice was forthcoming. These ideas were brought to a head when I was consulted by a fellow worker at the National Institutes of Health whose chronically progressive retinal disease was under study at the National Eye Institute. Neither her ophthalmologist nor anyone else had ever mentioned to her such readily available adjuncts as large-print books, the large-print edition of the New York Times, or any of the many aids to the visually impaired. I therefore wrote of my own experiences and sent the manuscript to my own ophthalmologist, requesting his recommendations as to the best place to publish it. Receiving no answer to my request, I mailed the manuscript to the New England Journal of Medicine where, rather to my surprise, it was accepted and published. There resulted by far the largest wave of correspondence and telephone calls that any publication of mine has ever elicited. Many of the respondents were either visually impaired or were relatives of visually impaired persons. Some were ophthalmologists and a few were physicians in other specialties. Most of the letters were supportive and friendly and many recounted experiences which paralleled my own. It thus appears that failure on the part of the ophthalmologist to direct his blind patients to agencies which may improve the quality of their lives is not an isolated phenomenon. On the contrary, it appears to be quite widespread. Furthermore, as some of the writers of letters pointed out to me, the phenomenon is not peculiar to ophthalmology. Indeed, in many fields of medical specialization it seems that the specialist, once he has given all possible consideration to his particular organ or organ systems,

feels little further responsibility for his patient. "This man is blind and there is nothing that I can do for him." "This woman has multiple sclerosis and there is little or nothing that I can do for her."

In my judgment, this situation arises in part from the exorbitantly rapid rate of growth of medical knowledge. It has been estimated that the growth of medical literature and therefore of medical information is exponential, with a doubling time of approximately 12 years. This means that in 48 years, which may be the approximate professional life of a physician, his subject matter has increased 16-fold. It is quite impossible for the physician to be expert in all aspects of a field that is growing at this rate. He therefore, perforce, specializes. He selects a narrow and ever narrower field in which he can remain truly expert. It is, I believe, quite appropriate that each doctor wishes to deliver to his patient the very best, the most modern, the most comprehensive knowledge upon which to base his diagnosis and treatment--but he pays a price for this specialization. Because it consumes all of his intellectual energy to keep up with his field, he has no energy left over to look at and to consider the remainder of his patient. More and more he tends to treat the disease of his specialty rather than the person who has come to seek his aid.

In part, our system of medical education is to blame for this attitude. The faculties of most medical schools are heavily loaded with specialists. True, today on most faculties there are representatives of general practice, of primary care physicians. But these, I suspect, do not engage the imaginations of most of the medical students. The typical role model for a medical student is likely to be the cardiologist, neurologist, or orthopedic surgeon who is at the leading edge of the science of his specialty. He is most likely to engage the respect of the medical student to serve as prototype.

Specialization has become the practice in many fields. Typically the performing musician is at home on one instrument but not on all. We do not expect the clarinetist to be a good percussionist. The one-man band, an occasional vaudeville act of many years ago, has long since disappeared. Similarly, if the family car needs repair we select a transmission expert, a body-and-fender man, or an authority on electrical components, depending upon the diagnosis. The universal auto repairman is today a rarity and in another generation will have disappeared.

In music, we have in some degree offset the move to instrumental specialization by the invention of the conductor, who ideally must know something about all the instruments in the orchestra but need not be proficient on any one of them. His role is to synthesize. It would be my hope that a medical specialist corresponding to the role of the conductor in music may yet be created. He will, of course, have some elements of today's general practitioner. He should have special training in the presently neglected area of synthesizing information derived from many specialists. Clearly he must be a person of great wisdom and great compassion. For all of these reasons, he will be a rare bird. In reviewing the many physicians whom I have met during my career, I can think of only three who might qualify: William Castle, Walter Bauer, and Robert Loeb. They all thrived a number of years ago when the medical world was younger and medical science a great deal simpler. Whether their like can still be produced remains to be demonstrated.

This is the end of my book. I have tried to record some of my gratifications and some of my frustrations. I hope that my family and those of my friends who chance to see it find themselves fairly treated. Most of my contacts with people, most of my adventures, I have enjoyed and I have taken pleasure in recalling them. I hope to stay at my job as long as I feel that I am making a contribution, even though a modest one. When and if I am sidelined, I hope that I shall have the good sense to depart quietly, bearing in mind Milton's closing line, "They also serve who only stand and wait."