THE ROAD TAKEN

Barry L. Zaret

Early Years

I grew up in an East Coast fountainhead: Brooklyn, New York, in an area called East Flatbush. It's a place I suspect many in this organization know or have known. The neighborhood was the equivalent of a *shtetl* when I lived there. Each street was like a little Jewish village where everybody knew all about everybody else. My street was composed of small buildings, each containing four apartments. Every two buildings were attached to each other on one side, like Siamese twins. Each building pair was separated from the next by an alley wide enough to park one car. There were clotheslines crossing the alley from one house to another. The clothesline was a metaphor for the connectivity that extended on the street. Conversations between neighbors and friends were carried out from windows across the alleys throughout the day. It was a friendly lower-middle-class neighborhood. Often individuals were identified by their profession. For example, my father was known as Irving, the butcher. The street was a "village" long before Hillary Clinton made the term famous. I grew up as an only child, somewhat over-protected and a bit sickly during my early youth, with lots of allergies and frequent respiratory infections, but nothing too serious. As a result, I missed a lot of school days due to illness and spent a lot of time alone.

My father had come to the United States from Belarus in 1928 at age twenty, after being orphaned at age nine or ten. Most of his large family had been killed in a pogrom in 1917. Only he and two sisters survived. It was remarkable how he overcame the extensive horror and trauma of his early youth to become an unconditionally loving, gentle, and caring human being. He became a U.S. citizen in 1937. He was a butcher who owned or worked in a number of small kosher butcher shops in Brooklyn and later in Queens. He would later joke frequently that he and I were both M.D.s: his son was a doctor and he was a meat dealer.

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My mother was a first-generation American. Her parents had immigrated to the United States from Galicia. According to social customs at that time, it was quite scandalous that she, as a native-born American, would marry a recent immigrant. But my parents were very much in love, overcame that somewhat Victorian viewpoint, and had a wonderful marriage that lasted over fifty years.

When I was eleven we moved from Brooklyn to Far Rockaway, a suburb of Queens. Far Rockaway was a small summer resort town known for its Atlantic Ocean beaches. We occupied a relatively small one-bedroom apartment in a six-story building located one block from the beach. It was part of a large complex of similar buildings. My life underwent significant changes shortly after we moved. My allergies and other illness significantly abated. I also found many friends among the boys living with their families in the apartment house complex. As I entered adolescence, there were lots of activities, a newfound interest in sports, as well as girls.

After graduating from our small elementary school, I entered the local high school. High school academic activities were something I didn't take too seriously or work too hard at. I found it relatively easy and not generally inspiring. At this time in my life I was having lots of fun and was truly enjoying my new life. I also longed for independence as I emerged as a teenager. As a result, I began working in the summers to earn spending money. My first employment, at age fourteen, was as a caddy at local golf courses. At age sixteen I began working in a local grocery store during the summers as well as after school. My high school grades were fine, but not sensational. I apparently did have early creative tendencies. When recently reviewing my senior high school yearbook, I rediscovered two poems I had written that were published there. I had also illustrated one poem with a pen-and-ink drawing.

Queens College

At the beginning of my senior high school year it was time to consider a college education. The only decision presented to me by my parents was which of the tuition-free local commuting city colleges of the City University of New York I would attend. My parents did not have the resources to send me to a private university. Furthermore, it wasn't part of either my family or personal culture to consider applying for scholarships or loans. Consequently, I followed the example of an older cousin who was attending Queens College in Flushing, New York. I commuted to this college for four years. The trip was about an hour and a half each way. The commute was accomplished by joining a carpool with fellow students who had access to a vehicle, or by public transportation, which involved taking multiple buses. By commuting to college, I missed the personal growth opportunity associated with living away from home. But I did have an active social life there. I joined a branch of a national college fraternity and in my senior year served as its president.

At Queens College I discovered the joy of learning. An entirely new intellectual world opened for me. At that time Queens College had a very rich core curriculum modeled after the Columbia University undergraduate program. It contained

extensive liberal arts and social science requirements. There were also requirements for foreign language studies. It was a comprehensive and wonderful education which I still look back on with the greatest fondness. This was a time of intense intellectual awakening. I became immersed in literature and art as well as science. I suddenly loved learning for its own sake. This was an immensely exciting time.

At the onset of matriculation, I wasn't sure what field I would be interested in pursuing. As a result, I once again followed my cousin's lead and selected chemistry as my major. He was three years older and was already committed to a career in chemical research and academia. After my first year, I realized that I did not wish to become a chemist. However, I was interested in science and continued with chemistry as my major, with a minor in biology. I also took as many elective literature courses as possible.

On my first day at Queens College, while registering for classes, I met a young woman named Myrna Zimmerman, who was to become my wife of forty-seven years. She too was to become a chemistry major. There was an instant attraction and we began dating as freshmen. We shared many classes together over the next four years. Our relationship became very serious. We became engaged in our senior year and were married one year after college graduation.

During my sophomore year, I viscerally began to feel that the field of medicine was something I would be interested in. At first, this surprised me. I had no physician role models, either in or outside my family, and there were no family illnesses that emotionally could have propelled me into medicine. Nevertheless, I was attracted to the field and to the concept of caring for and healing people. My excitement in my studies was translated into excellent academic performance. I did very well in my classes, leading to induction into the Phi Beta Kappa Honor Society as a junior. I subsequently graduated *summa cum laude*. At the onset of my fourth year I applied to several medical schools and was accepted to most. Fortunately, I received a full-tuition merit scholarship from New York University School of Medicine (tuition at that time was $2,500/year). This removed my parents from any financial burden. I gladly accepted this position. The scholarship also meant that Myrna and I could marry and support ourselves on her salary while I was a medical student.

During my college years, I continued working each summer. For the first two summers I continued in the local supermarket. For the last two summers I found employment in the local post office. Since Far Rockaway's population expanded with tourists in the summer, extra help was needed for mail delivery. Several of my friends also worked in the post office these summers. While they were lucky enough to deliver mail, thereby enjoying the Far Rockaway sunshine during the workday, I was assigned to sorting mail on the indoor midnight shift. I worked from midnight to 8:30 in the morning. As a result, during the work week, I lived totally out of phase with the rest of my environment, Myrna, family, and friends.

After college graduation, during the summer before the start of medical school, I continued post office work. At that time, I found myself in the throes of a new acute intellectual panic reaction. I was concerned that, since I was now committed to the

study of medicine and to being a physician, the rest of my life would be consumed primarily with the study of medical literature. There would be little time remaining for the other literature that I also loved. Since I worked all night, after a brief rest in the morning, I had the rest of the day free. Making the most of this odd schedule, I began an aggressive daily campaign of summer reading while sitting on the beach. I consumed about fifteen to twenty books during that period. They were all classic works from various time periods. Fortunately, this intense endeavor did not produce sunstroke. But it did alleviate my early cultural anxieties. Fortunately, the anxiety was unjustified; I was able to continue my outside interests throughout my medical career. In homage to that time, for many years I have worn a T-shirt with the inscription "*So Many Books, So Little Time.*"

Medical School

In September 1962 I began my medical studies at New York University. It was a very exciting and stimulating place then, as it remains today. For the first year I lived in the school dormitory. At the end of the first year, Myrna and I were married. We then moved to our first apartment, a small one-and-a-half-room studio on the Upper East Side. She was able to walk to work at Sloan Kettering Medical Center, while I took the bus back and forth to NYU. That era was a remarkable time in both medicine and in the medical school. The first-year curriculum included biochemistry. In addition to the classic biochemical teaching, there was intense lecturing on the newly discovered genetic code, which was just beginning to be understood. I still remember the image of the chairman of biochemistry, the Nobel laureate Severo Ochoa. He would approach the podium in the large lecture hall, his long white hair flowing, wearing a white laboratory coat, sandals, and an open shirt without tie. He was my image of a scientific Olympian. I sat in awe while busily taking notes and absorbing new concepts, the undifferentiated but very excited Brooklyn boy learning at the feet of a master and a Nobel laureate. One of Ochoa's postdoctoral fellows was Peter Lengyel. Peter later was recruited to the Yale faculty and now is also a member of the Koerner Center. He also lectured to our class on the basics of genetic code analysis. He included his very exciting research results. Peter gave some of the best lectures in the course. In my second year, I was further inspired by another Nobel laureate, Dr. Baruj Benacerraf, who received the prize for his work in basic immunology.

In the first two years of medical school we were taught to think scientifically. The only rote memorizing occurred in the study of anatomy. The rest of the basic science curriculum focused on "cutting-edge" topics and was very exciting. At the end of my second year at NYU I was offered a summer research scholarship. At this time, I wanted to begin to learn about how to do investigative work. The first two medical school years had helped me focus on what I thought I wanted to do in the future.

I was placed in the laboratory of Dr. Fred Becker, a dynamic young assistant professor in the Department of Pathology. Fred went on to have an illustrious career as a scientist and was subsequently named president of the renowned MD Anderson

Cancer Center in Houston, Texas. Working with Fred and his technician, I acquired enough data that summer for my first scientific paper. Its title was "Regeneration of the Mammalian Liver III: Electrokinetics of Replicating Cells Treated with Anti-Mitotic Antibiotics." I was quite lucky to have acquired meaningful results in initial experiments. We then performed concluding experiments over the following year and were ready to start working on a manuscript. The project involved studying regenerating rat liver cells following removal of a portion of the liver. We evaluated the surface electrical properties of these cells during the regeneration period. It was surmised that there was change in the net electrical charge of these cells and that this may have played an important role in motility and regeneration. Our experiments involved treating rats who had undergone partial liver removal with substances that would decrease protein synthesis. The liver cells were then harvested and their migration in an electrophoretic field studied. In addition to regenerating rat liver cells, we also studied rat cancer cells as controls. My first paper was published shortly before my graduation in 1966.[1]

After two years of a basic science curriculum, the last two years were spent learning the art and science of clinical medicine. While taking part in this endeavor, I became aware of how easy it seemed to learn the patient-oriented clinical disciplines. This was not an educational chore, but a natural process. Whatever the initial stimulus, clinical medicine was a most appropriate choice. Whatever the reasoning or lack of reasoning, this was the field meant for me. In medical school I again did well with respect to the metrics of rank and class standing. I was inducted into the Alpha Omega Alpha Medical School Honor Society during my junior year.

There were a number of important mentors and role models during the clinical years of medical school who significantly influenced my subsequent career choices. My medical "father figure" was our professor of medicine and chair, Dr. Saul J. Farber, a major force in internal medicine at this time. One of my teachers was Dr. Jerome Lowenstein, a consummate clinical physiologist, nephrologist, and clinician. He later founded one of the first programs in humanities of medicine at NYU. Both men instilled in me the unique excitement of combining clinical excellence and clinical research. They stressed inquisitiveness and curiosity, always asking questions at the bedside that could lead to new research questions into the study of disease.

I encountered two other physicians who would not be found in the pantheon of academic physicians, but who significantly influenced my approach to clinical medicine and patient care. Dr. Marcel Tuchman was a Holocaust survivor and a full-time practitioner. He was the most empathic physician I ever met. He became my role model with respect to how I wished to approach patients and care for them. The other was Dr. Joseph Brumlik, who was a practicing cardiologist and one of the last pupils of a European pioneer of electrocardiography, Karel Wenckebach. Brumlik was a masterful old-style, old-world clinician. He maintained an active interest in cardiology and disturbances of heart rhythm. It was his practice to have a medical student collect all the cases of serious arrhythmias encountered during the previous week on

the wards of Bellevue Hospital. These cases would then be presented to him and his entourage by the student at rounds on Saturday mornings. I was given the opportunity of having this job with Dr. Brumlik in my fourth year. Over the course of that year I learned much about heart rhythm disturbances, while also receiving a small stipend. This work further stimulated my interest in cardiology.

The mid-'60s was the period when the Vietnam War was beginning to accelerate, and there was an active military draft. Medical students received draft deferment while in medical school, but had to register with the local draft board as graduation approached. I spent many sleepless nights wondering if I would be sent to Vietnam. In the final year of medical school many of us applied to the National Institutes of Health for Public Health Service positions in laboratories at the NIH. This service would fulfil our military obligation. With many other students, I traveled to Bethesda, Maryland, to be interviewed for an NIH position. I hoped to go to the National Heart Institute, but I was not offered a position there. However, I did get an offer to work in a laboratory at the National Cancer Institute. The laboratory director was interested in the work I had done during my summer research project with Fred Becker. By that time I had developed an interest in cardiology and knew that was the field I wished to pursue. An additional drawback of the NIH position was that I would have to begin immediately after completing my internship, without obtaining full training either in internal medicine or in a subspecialty. However, with no other viable option, I accepted the position.

The Vietnam War also impacted directly on my graduation experience. As our June 1966 graduation drew near, members of our class learned that NYU was to offer an honorary degree to Robert McNamara, then Secretary of Defense and an architect of the Vietnam War. The awarding of the honorary degree was to occur at the university-wide graduation ceremony, which at that time took place at the large NYU campus stadium in Washington Heights. Our medical school ceremony had occurred the previous day in a different location. A number of individuals in our class were very upset about McNamara receiving this honor. As a result, a walk-out protest was organized to take place when McNamara's name was announced for the honorary degree. Some of the student leaders came to me and asked that I join them. I was not a political activist, but I felt strongly about this issue. I agreed. Our plan had been discussed with Dr. Farber, our mentor, who was then also acting dean of the medical school. It was agreed that we would walk out of the graduation, but would then be allowed to return and take part in the rest of the ceremony, including the administration of the Oath of Hippocrates. On the day of graduation, when McNamara's name was called, our group stood up, and perhaps a quarter of the medical school class walked out, accompanied by other students from different schools of the university. What happened next remains etched in my memory. As we exited the stadium, each of us was individually photographed by a team of FBI agents who observed us quite carefully. After we left the stadium, the gate was closed. We were not allowed to return.

Afterward I had to explain to my mortified parents that their only son, the realization of the immigrant dream, was still to be a doctor, that he had graduated, and that he would continue his career. They were anxious, confused, and very worried! Years later I wondered if this event would impact my ability to receive federal funding. Fortunately, that was never the case. Perhaps sometime in the future I will request my personal file (if one still exists) from the U.S. government by invoking the Freedom of Information and Privacy Acts.

Internship and Residency

On July 1, 1962, I began my internal medicine internship at Bellevue Hospital in New York City. At the start of the year I also received a U.S. government communication indicating that each of the branches of the military (Army, Navy, Air Force) had identified the number of medical specialists required to meet its medical needs. A lottery (the Berry Plan) was established that would select the requisite number of individuals in each medical specialty for each service branch. The selected individuals then would be deferred in order to complete full training as a specialist. Thereafter they would immediately enter the military and serve their two-year commitment as medical specialists. The announcement also provided statistics showing the relative chances of getting a position in each specialty in each of the three military branches. As I perused this communication, I noted that for draftees pursuing a career in cardiology, there was a 50 percent chance of getting a deferment in the Air Force. By this time, I was committed to becoming a cardiologist. The thought of spending two years doing research in oncology, although far better than being in Vietnam, was not my first choice. I therefore entered the lottery, selecting cardiology as the field and the Air Force as the military branch. Fortunately, I was selected. There was no problem with canceling plans for spending two years at the National Cancer Institute. My chairman, Dr. Farber, was also delighted with this outcome. He immediately indicated that there would be a spot for me to complete my entire three-year internal medicine training program at Bellevue.

Bellevue Hospital was the largest of New York City's municipal hospitals and was the major teaching hospital of New York University School of Medicine. The hospital serviced New York's acutely ill, its poor and underserved populations. It was a sought-after training program, despite its physical rigors. The work was extremely intense. As an intern, in addition to the routine five-and-a-half-day week, I was on call and stayed in the hospital every other night and every other weekend. We had only a day and a half away from the hospital over each two-week period. Although I've never worked as hard physically as I did during that year, the rewards and the learning were enormous. There was a lot of responsibility in patient care as well as in the teaching of medical students. I was amazed at how the body adjusted to getting by on very little sleep. Fortunately, Myrna was very supportive and understanding during that very difficult internship period. Our marriage survived and even thrived, despite the fact that I was home so infrequently.

During the following year of training, as a first-year resident physician, my responsibilities increased significantly. I was in charge of a patient ward for the majority of the year. There were two interns working with me, as well as a group of four to six medical students. I jumped at the opportunity. I found time to keep up with the journals, to learn, take care of my hospitalized patients, as well as have an outpatient clinic once a week. I found that I loved teaching and loved the responsibility of being in charge. We were supported and taught by wonderful attending physicians who would round with us daily. They were superb teachers and role models. But, the patients on the ward were the house staff's patients; we accepted that. I learned quickly to do whatever was necessary to ensure their best outcome. At times, in addition to medical care, this meant wheeling patients to the x-ray department at 3 a.m., doing routine lab work, or administering medications in the middle of the night.

At the beginning of my final year of training, our oldest son, Adam, was born. Fortunately, this occurred when my on-call duties in the hospital were reduced to every sixth night and every sixth weekend. It felt positively luxurious to have more time to spend with Myrna and our new son.

During my second year of training at Bellevue, I became friendly with a third-year resident, Bill Strauss, who had transferred to Bellevue for his final year of training from Kings County Hospital in Brooklyn. We worked together and quickly became close friends. At the end of the year he left to begin an advanced training program in the relatively new field of nuclear medicine at Johns Hopkins Hospital in Baltimore. Quite fortuitously, the next year, after going through intense interview processes at several hospitals, Johns Hopkins was my first choice for cardiology training. I was accepted to the program, and in June 1969 we left New York City and moved to Baltimore. Five months later our second son, Elliot, was born.

Cardiology Fellowship

Having spent my entire life to that point in one of three boroughs of New York City, finding myself in Baltimore was like entering the deep south. I quickly overcame both the culture shock and my New York provincialism and began to enjoy living in Baltimore, interacting with my new colleagues and taking part in the excellent cardiology training program at Johns Hopkins. The two years at Johns Hopkins were critical for my development. I was now learning my future new field in depth. I was transitioning to become a consultant and a subspecialist. The learning curve was steep and exciting and reminded me of the learning gradient I experienced as an intern. I was also about to have my first experience in clinical research.

Hopkins was a very austere institution filled with lots of history. The environment was very proud of that heritage and took itself very seriously. Portraits of well-known, world-class physicians who had left their mark on medicine abounded on the Hopkins walls. When entering the medical center from the parking garage, one immediately encountered a rotunda containing a huge statue of Christ. This was my greeting as I

began each day at Hopkins – quite different from my Bellevue experience and quite a new world for a Jewish boy from Brooklyn.

The chief of cardiology and my senior mentor was Dr. Richard S. Ross. Dick was extremely bright, well-organized, honest, and always to the point. Hopkins was a very hierarchical institution; there was no doubt that he was the boss. He subsequently was named dean of the medical school at Hopkins and oversaw a significant period of growth at the school. My research mentor was Dr. Bertram Pitt. At the time, Bert was a young assistant professor, very creative and intense, always bubbling with new ideas. Bert went on to an illustrious research career and also became chief of cardiology at the University of Michigan, where he remains active in clinical research at the time of this writing.

As mentioned above, my co-resident and friend Bill Strauss was in nuclear medicine training at Hopkins, under the guidance of Dr. Henry Wagner. Henry was a pioneer in developing this discipline, which involves the use of radioisotopes, much as radiologists use x-rays, to define clinical, diagnostic, and physiologic phenomena.

My work as a cardiology trainee was once again very demanding physically and mentally, although not nearly as severe as the Bellevue years. I was learning a new field and also learning how to perform multiple advanced techniques and procedures such as cardiac catheterization, angiography, and pacemaker placement. While at Hopkins, I also encountered a chief resident in internal medicine, Tom Duffy, who subsequently was recruited to the Yale faculty, where he has been a colleague for many decades. He is now also a valued colleague at the Koerner Center.

In addition to learning clinical cardiology, I had the opportunity to spend about a quarter of my time in the research laboratory. I began my project under the direction of Bert Pitt. Bill Strauss collaborated in these studies since the work involved using radioisotopes and nuclear medicine techniques. We started with a series of physiologic experiments to study coronary blood flow in dogs, using radioactive Xenon gas dissolved in saline and injected into the coronary arteries of dogs. Our aim was to visualize and quantitatively study the regional washout of this radioactive material from the heart using a newly developed radiation detector called the scintillation camera. From the washout curves, we could mathematically derive regional coronary blood flow. We did many preliminary experiments that helped standardize the animal model. These experiments could only be done at night, since the equipment was used during the day for patient studies. We would start at about 7 p.m. and often continue until 1–2 a.m. The preliminary studies went well. However, we soon reached an impasse while waiting for a computer interface to be built for the scintillation camera. This was in 1969, before the routine use of computers and digitization of visualized data. The computer scientist assigned to this task was continually delayed in delivering the promised work. As time passed, I became despondent – I saw my valuable research time passing quickly, with no immediate hope of performing the key experiments for which we had done all the preliminary work and developed the animal model.

One night after finishing a study, Bill, Bert, and I brainstormed. Bert mentioned that perhaps we should change direction, rather than continuing to tread water waiting for the technical development to arrive. He suggested studying a relatively new measurement of heart function that at the time could not be obtained simply and noninvasively. This measurement was called left ventricular ejection fraction (LVEF), which is the percentage of left ventricular volume ejected with each heartbeat. We planned to detect radiation only during selected parts of the cardiac cycle, as determined by the simultaneous electrocardiogram. In so doing, we could measure the amount of radioactivity in the heart when the left ventricle was at its largest point (end-diastole) and again at its smallest point (end-systole) and sum the selected data over several hundred heartbeats. By having that information, we could utilize a straightforward formula for measuring ventricular volumes, and from the volumes, determine LVEF, a measurement of heart function. We did preliminary experiments in dogs, using albumin labeled with radioactive technetium. This was injected intravenously and remained in the bloodstream during the period of study. This was an important property of the radioactivity since it allowed us to sum the radioactive data from multiple heartbeats at either end-diastole or end-systole. Our initial animal experiments went well.

We quickly moved to man. The human studies also went well. By superimposing radioactive images at the ventricle's largest and smallest volumes, we could also assess the wall motion of different portions of the left ventricle. We were able to correlate our measurements with those made in the same patients in the cardiac catheterization laboratory, where the information was obtained invasively by placing a catheter within the left ventricle and injecting radiopaque dye. Our correlations were excellent. This was the first demonstration of obtaining valuable quantitative clinical data noninvasively, without performing cardiac catheterization and angiography.

Our work was presented at several national scientific meetings and was published promptly as two separate papers.[2, 3] The measurement ejection fraction is still used today and has retained its clinical value. Our technique was soon used to study patients who were in a special myocardial infarction research unit at Johns Hopkins. The measurement then was employed widely, was used nationally and internationally, and became a part of routine clinical practice. LVEF is now obtained noninvasively using a number of different techniques. While presently this measurement is infrequently done by nuclear techniques, it is very commonly measured by echocardiography.

The two years at Hopkins passed very quickly. I was then ready to enter the Air Force and fulfill my draft commitment by serving the next two years as a U.S. Air Force cardiologist.

Travis Air Force Base

As a result of my Berry Plan deferment, I received my military appointment with the rank of major. I was stationed at Travis Air Force Base in the Sacramento Valley,

California, an ideal location about an hour by car from San Francisco and just across the hills from Napa Valley. We lived in a small house on base in the officers' housing area. The hospital was one of the seven major referral centers of the U.S. Air Force Medical Corps. It was well equipped and also had a training program for interns and residents, who were considered active-duty military personnel while receiving their medical training. The medical staff—two-year transients like myself, as well as career Air Force physicians—were excellent. The hospital was also located a half hour by car from the medical school at the University of California, Davis. The cardiology staff were given adjunct faculty appointments and frequently interacted with the full-time faculty there. In many ways this was like my first faculty job without the tenure clock running.

The cardiology group consisted of five physicians. We all worked very well together. Much to my pleasure, Bill Strauss had also been assigned to the same hospital. He was involved in clinical nuclear medicine, just as I was involved in cardiology. After all of the anxiety that had gone into the possibilities of being sent to Vietnam or other small U.S. hospitals of lesser stature, I was now at a superb institution with a strong academic orientation and excellent colleagues. There was also the collateral benefit of living in Northern California for two years. I had been dealt a wonderful hand, particularly in light of the alternatives.

Over this two-year period, from a clinical standpoint, my work involved almost exclusively cardiology. We had an active cardiac catheterization laboratory where I performed procedures and studies at least once a week. I also had several clinics which were filled almost exclusively with cardiac patients, both active-duty and retired personnel. I also enjoyed teaching internal medicine and cardiology to our interns and residents. The contact with UC Davis medical school was also stimulating.

While in California, Bill Strauss and I wanted to continue research, despite the fact that such activity was well beyond the Air Force Medical Corps' job description. We began thinking if it would be possible to begin clinical investigative studies suitable for performance in this particular environment. By this time, having worked with radioisotopes in heart studies over two years at Hopkins, I wanted to continue in this particular genre of clinical investigation. At the time, the field of nuclear cardiology didn't exist. I knew I wanted to play a role in placing it on the clinical map. Bill and I speculated about using a different radioisotope that would be taken up by the heart when injected intravenously. This uptake would have to be proportional to blood flow in various regions of the heart and would allow visualization and ultimately quantification of any portions of the heart that were not receiving adequate blood flow. Some very preliminary studies in this area had been done by others, predominantly in experimental animals. A few patients had been studied in the resting state. These studies involved human or experimental myocardial infarction (heart attack). We thought it would be highly relevant to inject the radioisotope while the patient was exercising on the treadmill and by doing this, detect portions of the heart that were not getting

adequate regional blood flow under conditions of stress. That would mimic the clinical condition seen in patients, namely myocardial ischemia or angina pectoris. Most of the time, except when people are having heart attacks, the chest pain that they experience does not occur at rest.

To do this we needed a radioisotope to be injected intravenously and then taken up by heart muscle. The only such radioactive tracer available at the time was a radioactive form of potassium (potassium-43). This was only being made by Cyclotron in Oak Ridge, Tennessee. However, a commercial company, Medi-Physics, had just decided to begin producing this material. Their operation was in Berkeley, California, forty-five minutes from Travis Air Force Base. Bill and I met with the Medi-Physics team and they agreed to work with us, providing we could develop funding to cover the cost of the radioisotope. Fortunately, I was able to apply for a grant from the Air Force Surgeon General's Office. We were approved and received enough funding to obtain initial shipments of the radioisotope.

We started the initial exercise studies as soon as the grant was activated. These studies went very well. When we injected the radioactive potassium-43 intravenously into an exercising patient, we could subsequently visualize areas of the heart that didn't receive enough blood supply and consequently had decreased radioisotope taken up. There was a "hole" in the heart that was reflected in the scan obtained. When we repeated the same study with the patient at rest, and not having any symptoms, the uptake of the radioisotope in the heart was homogeneous. This was very exciting. We had coupled a physiologic principle with static radioisotope imaging. As a result, we could visualize ischemia for the first time in man. We then did a series of studies in patients who had undergone coronary angiography.

These studies corroborated the scan findings: there were narrowed coronary arteries seen on angiography that supplied the heart regions with decreased isotope uptake. The results were published in the *New England Journal of Medicine*.[4] This work on myocardial perfusion, coupled with our initial work on measuring heart function, set the stage for nuclear cardiology becoming a new discipline. We soon had visitors from academic centers coming to our small military hospital to learn the principles and practicalities of this new approach. The two years in the Air Force turned out to be extremely exciting. I was able to publish five papers dealing with various aspects of this technique in different clinical populations. We were able to do other studies, collaborating with Medi-Physics, which included examining other new radioactive tracers that might be used for such studies. We were able to do animal studies as well.

During the second year at Travis Air Force Base it was time to consider the next phase of my career. I enjoyed both clinical medicine and clinical science and wanted to do both. I knew that I wanted to pursue a career in academic medicine. The unexpected success at Travis Air Force Base had established the basis for the new clinical discipline of nuclear cardiology. I wanted to pursue and develop this area in an academic environment. At the time, I received several offers to remain in California and enter both

private practice and academics. My heart was set on academics, and I wanted to return to the East Coast. When I had left Johns Hopkins, there had been informal discussions about returning and joining the faculty after the Air Force years. I remained in touch with my former chief, Dr. Richard Ross. In the fall of my second year in California, Dr. Ross was a visiting professor at Stanford University. He asked that I come to Stanford so that the two of us could meet. I was hopeful that this would be the beginning of negotiations for a position. Unfortunately, he informed me that there was no longer a faculty slot available at Hopkins. I was devastated by this realization. I felt isolated and removed from academia. At this time, we had two children, ages four and two.

Joining the Yale Faculty

My former research mentor, Bert Pitt, came to my rescue. He made introductory calls to several heads of cardiology academic programs around the country proposing me for a faculty position. One of the people he spoke to was Larry Cohen, then chief of cardiology at Yale. I interviewed in New Haven and gave a seminar on my new work. I was offered a position, which I promptly accepted. My two years of required military duty were concluded during the summer. In September 1973 I arrived in New Haven. Myrna and I had come East earlier to celebrate the Passover holiday with our family. During this time, we left our two children with their grandparents and spent several days looking for housing in the New Haven area. We found the one house we liked and promptly bid and obtained it. I was soon to become a Woodbridge resident.

After getting settled (Myrna, now pregnant, and the two boys had come earlier and were already in the house while I finished my tour of duty), I began working at Yale on October 1, 1973. I envisioned my stay at Yale as likely relatively short-term and transient. I thought this would be the first of many jobs. At that time academic medicine was often defined by ongoing professional mobility. In February our third son, Owen, was born at Yale New Haven Hospital.

My career began at Yale just as the field of nuclear cardiology was being recognized as a new "hot" area in cardiology. As such, funding for research in this area was quite good. After being on faculty one and a half years, I obtained grants from the NIH, the local Connecticut Heart Association, and the American Heart Association. With this funding I was able to establish my own research program involving both experimental studies in animal models as well as clinical investigation involving patients. When I started the animal experimental program, I worked initially with medical students who were pursuing their M.D. thesis requirement at Yale. They were very bright and energetic and authored several papers. For human studies I worked predominantly with our cardiology trainees. I began to transition from doing my own experiments to supervising others. This required significant adjustment.

The work went well, and the lab was productive. Four years into my career, I competed successfully for an Established Investigator Award from the American Heart Association. While developing my research program, I also had significant clinical

responsibilities. I spent about half the year involved in clinical service and teaching. It was becoming increasingly difficult to perform these activities at their current time commitment and do them well. I also needed to decrease these activities if I was to maintain my growing research program. At the onset of my career, as with other members of the cardiology faculty, I had a clinic where I cared for my own patients. I continued this practice throughout my career. At that time, the cardiology faculty, as the faculty of the medical school in general, was relatively small. I believe there were only about seven cardiology faculty covering both Yale and the West Haven Veterans Administration Hospital. It was clear that I needed additional faculty support if I was to pursue my research career at its present level. In view of the fact that I had significant funding, I was able to lobby to bring an individual with an interest in nuclear cardiology to the program. With a bit of luck and lots of persuasion, I was able to recruit a Dutch cardiologist, Frans Wackers, from Amsterdam. He had just started his career in nuclear cardiology and recently completed his general cardiology training. He had already done important clinical research in the coronary care unit involving imaging patients with acute myocardial infarction. He was able to join us in 1977–78 and, with the exception of his brief two years at University of Vermont, has been a close colleague and friend ever since.

Chief of Cardiology

In 1978, after five years on faculty, I was asked by the chairman of the Department of Internal Medicine, Dr. Samuel O. Thier, to assume the position of chief of the Cardiology Section. This was a somewhat difficult decision since my research career was growing rapidly. Taking on the leadership role in cardiology would no doubt impact current research productivity. I had quite unexpectedly found myself in a pool of candidates considered for such positions around the country. I had been asked to interview for several positions. I hadn't pursued any of them seriously. However, I reasoned that staying at Yale where I had an investigative program already in place could in part counterbalance the time that would have to be spent in leadership and administration were I to take on a new position. With the arrival of Frans, I would have a very good partner to collaborate with and share responsibilities. From a social standpoint, Myrna and I were fond of our new community and our proximity to families in New York. We now had three young children. We were not enthusiastic about moving. A decision had to be made.

Consequently, with trepidation, I accepted Sam Thier's invitation. Sam was a brilliant leader who was incisive, intense, charismatic, honest, and incredibly smart. He became my administrative mentor as I began navigating this new role of leadership at a relatively early time in my career. Sam was a splendid role model; he influenced me greatly in my new role. When Sam left Yale, he went on to have a remarkable career, which in addition to several very important positions in medicine, included being president of Brandeis University.

At this time, I was receiving many invitations to speak nationally and internationally. The field of nuclear cardiology was new and was regularly featured in postgraduate cardiology symposia. One of the most interesting and meaningful invitations involved a return to the Far Rockaway area where I had grown up. A relatively small local hospital organized a symposium on nuclear cardiology. I was asked to be a featured speaker. The organizing committee arranged for my parents to be invited to hear my lecture. Up to this point, they had never quite understood my career. It didn't relate to any of their systems of reference. I had become a physician, but I was not in full-time practice. I didn't drive a fancy car. I spent time experimenting on dogs in the animal laboratory. I only saw patients one day a week, unlike any physician they knew. I worked with radioisotopes, which they knew from world news were dangerous. In short, I was a medical anomaly to them. I had sent them copies of many of my papers. They politely accepted them; but I'm sure the papers were never read. However, now I was invited back to their hospital, Peninsula General Hospital. They were given VIP treatment, ushered to seats in the front row, and heard me lecture for the first and probably last time. Suddenly it all made sense. That I had already lectured in the Ether Dome at Massachusetts General Hospital didn't matter to them. For the first time, they saw my career in a metric they could relate to. They never again asked why I didn't drive a Cadillac.

On July 1, 1977, three months before my thirty-eighth birthday, I officially became chief of cardiology at Yale. I was charged with further building the research and clinical program. My first thrust was to recruit young faculty that would diversify our research portfolio, since at that time the predominant aspect of research in our section involved nuclear cardiology. I had not had experience in administration, financial aspects of running an academic program, or leadership outside the boundaries of my own research program. This was anxiety-provoking new ground, and there were many sleepless nights spent wondering about the wisdom of going down this administrative path, especially considering that my research program was going so well at the time. I now found myself responsible for the educational aspects of our training program, the growth of our clinical program, the expansion of our research, and the fiscal aspects of managing the entire operation. About three or four months into the process, the stress was beginning to take its toll.

It was at that time that I began long-distance running as a method of stress modification. Soon I was totally committed to this activity and gradually expanded my efforts to five- and ten-kilometer road races and taking part regularly in the twenty-kilometer annual New Haven Labor Day Road Race. In following years, I completed three full marathons (26.2 miles). I have never deviated from running and exercise for the past forty-two years. Currently I no longer run outdoors, but use a gym in our home basement equipped with treadmill, elliptical trainer, and stationary bicycle. I use my facility about five times per week.

After the first years of settling into the job as section chief, I began having increasing levels of comfort. In 1982 I was appointed a full professor and in 1984 I became the

first Robert W. Berliner Professor of Internal Medicine. I remained as section chief for twenty-six years. With experience, faculty expansion, and delegation of responsibilities, the job became manageable. Working with Frans Wackers, a very productive program was built in experimental and clinical nuclear cardiology. The clinical laboratory soon became a major component of cardiac testing within Yale New Haven Hospital. My research continued, although with less hands-on effort. I was delighted to have Frans as my partner and friend. We have continued that throughout both our careers and remain friends in retirement.

My research involved further studies in the use of radioisotopes for evaluating cardiac function, blood flow, and metabolism. The lab remained productive and recognized for its expertise. Many of my studies involved basic physiology as well as clinical studies. Frans and I also demonstrated the concept of using core laboratories to take part in major large clinical multicenter trials involving thousands of patients. In these large studies, the core lab processes large volumes of nuclear data from a multitude of centers. The data, which are important parameters for the trials, must be quality controlled, interpreted, and reported in a timely fashion. We started the first Thrombolysis in Myocardial Infarction (TIMI) Core Laboratory studies and expanded to other areas as well. Based on our results, other laboratories also took part in these core functions involving the use of nuclear data as part of large clinical trials.

Our laboratory was visited regularly by individuals from around the world. It was a pleasure to host both visiting professors and research trainees from diverse locations such as India, Israel, Egypt, and Canada, to name a few.

Over my years as section chief, the field of nuclear cardiology also grew dramatically. I was active in the formation of the American Society of Nuclear Cardiology (ASNC) and was named founding editor-in-chief of its *Journal of Nuclear Cardiology* (*JNC*), a position I held for two terms (ten years). I enjoyed editing the journal and used my editorial office as a bully pulpit to point the field in new directions, such as molecular imaging. With my colleague and friend Dr. George Beller of the University of Virginia, we edited a major text in nuclear cardiology, which is currently in its fourth edition and remains a standard in the field.

With the further development of nuclear cardiology, I had frequent invitations to take part in symposia, large meetings, and lectureships both nationally and internationally. This was and has been a very exciting activity. It has allowed me to develop long-standing friendships with individuals throughout the world and to help organize many meetings that sought to address the future of the field and its new directions.

One of the most exciting aspects of being chief of cardiology at Yale was the ability to influence the training of individuals destined to become cardiologists, both practicing clinicians and academicians. Over the years I have been involved in training several hundred such individuals and have remained in close touch with many. Many have gone on to positions ranking them at the top of the field, as well as deans, departmental chairs, and chiefs of cardiology. I have enjoyed both rounding with them as a clinical teacher and mentoring them as young investigators.

As stated, over time my administrative skills improved, and the section grew substantially. When I stepped down as chief we had over forty full-time faculty and a complex budget of approximately $20 million. As section chief I served under five departmental chairs and four deans. For the last twelve years as section chief I also was associate chair of clinical affairs for the Department of Internal Medicine and worked very closely with Ralph Horwitz, department chair. Expanding beyond the borders of cardiology also was satisfying.

I have enjoyed all the varying academic aspects of my career including serving on editorial boards, organizing academic meetings, peer review and study sections, and honorific societies. The most interesting meeting that I organized with two colleagues was called "Renaissance Perspectives in Nuclear Cardiology." This was a small meeting, by invitation only, and involved about thirty investigators. It was held in Tuscany, Italy. Participants were asked to speak on the state of the art and science of the field, to address future directions, and also to give a seminar that related to a nonscientific area of their choice. There was a wide range of topics chosen including history, poetry, art, and music. It was very memorable for all who attended.

Throughout my career, direct patient care was always extremely important. I maintained my clinic throughout my forty-five years at Yale until formally retiring one and a half years ago. Seeing and caring for my own patients on a weekly basis, following them in the hospital, getting to know them and their families have all been extremely rewarding. There are several patients I have cared for over forty years, despite their very significant cardiovascular disease. At times of maximal academic stress, my weekly clinic was always a time of occupational therapy, an opportunity for moments of reprieve and serenity. I tried to imbue my trainees with this joy of medicine and the importance of maintaining patient care and contact, rather than becoming technocratic and procedure oriented, as is so easy in the field of cardiology.

Perhaps the most rewarding clinical event in my life occurred in 1987. At that time my wife, Myrna, suffered a heart attack and cardiac arrest at our Woodbridge home in the middle of the night. I was able to resuscitate her and save her life, performing CPR alone in our bathroom. This happened on the evening of the Jewish holiday of Purim. Ten years after the fact, I was finally able to write about it in an essay called "Purim CPR."[5] The chance of having the success that occurred that night is probably one in a thousand. She never had another cardiovascular problem for the remainder of her life. Remarkably, she also maintained normal cerebral function after the event. Myrna lived thirteen years thereafter until she succumbed to lung cancer. I reflected and realized how my days at Bellevue had taught and prepared me to deal with something like that. It was at Bellevue that I learned how to function medically, immediately, in the middle of the night, almost at a spinal level. All the on-call nights of my medical youth more than proved their worth!

The Next Phase

I had planned to retire at age seventy and entered the early retirement program. But then a new realization hit: after I stepped down as chief, I was leading a life of less administrative responsibility and stress and I was very much enjoying just teaching, writing, and seeing patients. I wanted to continue at this pace and in this domain for several more years. Fortunately, I was able to stay on with the new title of senior research scientist, which I carried for my last seven years on faculty. I no longer continued an active research career, but I did teach in the Nuclear Cardiology Lab on a regular weekly basis, mentor colleagues and trainees, see my patients twice a week, and, importantly, continue to learn medicine.

During the past thirty years my life also expanded in different nonmedical directions. Through an unusual set of circumstances, I met Chaim Gross, a famous artist, sculptor, and painter. We became close friends. He also became my "artistic father." Artistic yearnings that had been suppressed during years of striving for academic and medical success suddenly rose to the surface. Chaim had unlocked a long-closed door. I started painting one summer while visiting Chaim at his vacation home in Provincetown, Massachusetts. He was no longer using his studio and casually said, "Why don't you start painting here?" I haven't stopped since. Myrna and I would visit him in Provincetown every summer as well as in New York City at his other home. In response to some of his artwork, I also began writing poetry, and this rekindled my interest in this art form. Painting and poetry have become two of my passions. I have worked diligently on them, without formal training, ever since. I have had two books of poetry published and many gallery art shows of my paintings, locally as well as in the Berkshires. This past May I had the wonderful experience of giving a poetry reading at the Gross House in Manhattan, which has now been turned into a museum for Chaim's art.

During my last seven years on the Yale faculty I tried to merge my interest in the arts with my interest in medicine and teach our cardiology trainees more about healing and humanities. I created a seminar program for them called "Humanities in Cardiology." This also included sessions on bioethics. I have been concerned about loss of empathy and loss of healing in medicine in the present era and have sought to teach and write about this.

As noted above, in 2010 my wife, Myrna, succumbed to lung cancer after twenty months of illness. I limited my activities at Yale for the last year of her life and devoted that time to her care. After Myrna died, I was very fortunate to meet Renée Drell. She and her late husband had been my high school classmates in Far Rockaway. We had lost contact over the years and met again through a fortuitous circumstance. With Renée I have found fresh new meaning in life. We have now been married for five and a half years. Our combined family consists of six children and eleven grandchildren.

I still maintain a desk and desktop computer in shared space in the Cardiology office area. I try to spend one or two days a week at Yale teaching, mentoring, learning,

and keeping in touch with my colleagues. I've truly enjoyed my career in medicine and at Yale. I feel it was a calling that I was fortunate to come to. I've never regretted a moment of it, though there certainly were many valleys present along with many peaks. It has been a great privilege to be a part of the excitement of healing and to witness the scientific advances in understanding and treating cardiovascular disease that have occurred during my career. It's been a delight to see patients with heart disease now often live long and relatively normal lives. This is so different from 1966 when I first cared for patients as an intern at Bellevue Hospital. New advances in medicine still excite me. It's remarkable how far we've come in such a relatively short time. I'll continue to enjoy medicine from afar, while still learning and pursuing other interests.

I'll end with a poem I wrote recently.[6]

On Retirement
The stethoscope rests quietly
in an antique desk drawer.
Once, always at my side,
now curled like a sleeping cat,
nose to tail.
At times the urge comes
to shake my lifelong friend
from its repose,
make it act again
as that special link
between ears and patient.
But desire soon passes.
Time has provided new means
to hear heart murmurings.

Notes

1 Barry L. Zaret, Lorraine R. West, and Frederick F. Becker, "Regeneration of the Mammalian Liver III: Electrokinetics of Replicating Cells Treated with Anti-Mytotic Antibiotics," *Proceedings of the Society for Experimental Biology and Medicine* 121 (Apr. 1, 1966): 1155–58.

2 H. William Strauss, Barry L. Zaret, Peter J. Hurley, T.K. Natarajan, and Bertram Pitt, "A Scintiphotographic Method for Measuring Left Ventricular Ejection Fraction in Man without Cardiac Catheterization," *The American Journal of Cardiology* 28 (Nov. 1971): 575–80.

3 Barry L. Zaret, H. William Strauss, Peter J. Hurley, T.K. Natarajan, and Bertram Pitt, "A Noninvasive Scintiphotographic Method for Detecting Regional Ventricular Dysfunction in Man," *The New England Journal of Medicine* 284 (May 27, 1971): 1165–70.

4 Barry L. Zaret, H. William Strauss, Neil D. Martin, Harry P. Wells, Jr., and M.D. Flamm, Jr., "Noninvasive Regional Myocardial Perfusion with Radioactive Potassium—Study of Patients at Rest, with Exercise and during Angina Pectoris," *The New England Journal of Medicine* 288 (Apr. 19, 1973): 809–812.

5 Barry L. Zaret, "Purim CPR," *Psychosomatic Medicine* 71 (Jan. 2009): 6–13.

6 Barry L. Zaret, "On Retirement," in *Craft, Verses, Inspiration: New Haven Poetry,* ed. Tony Fusco (West Haven, CT: Flying Horse Press, 2019).