Saul R. Korey and I: Reminiscence of New York in the early 1960’s


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How I got to New York

I graduated from the Faculty of Medicine, Tokyo University, in the spring of 1959. I had never intended to be a clinician but had decided on a career in medical research even before I entered the medical school. During my early undergraduate period, I was vaguely attracted to “some aspects” of brain research. My desire to study brain biochemically became clearer while I was working in Prof. Yukichi Kimura’s laboratory during my years as an undergraduate student in the section of History and Philosophy of Science of the College of General Education, Tokyo University. I worked on the then hot topic of the potassium effect using the Warburg manometer and rat brain slices. The potassium effect is a phenomenon discovered by Henry McIlwain that the oxygen consumption of brain tissue increases to 150% of the basal level when a brain slice is placed in a potassium-enriched medium. Outside of the lab, I was having the best two years of my life. I was free to follow my purely personal interests into all kinds of intellectual endeavors without any regard to potential usefulness in my future. In retrospect, I was experiencing the best of the true higher education without which my present is unthinkable. Sadly, this type of higher education is an endangered, if not already extinct, species these days when universities everywhere, not only in Japan but in nearly all countries, have forgotten the essential mission of universities and are striving to excel as trade schools.

I was not a good medical student. First of all, after the two years studying Philosophy of Science, medical school lectures just did not interest me. I felt that I was forced to digress to the previous century. Besides, I had too many distractions – mountain climbing and skiing, bird watching, photography, the Noh play, the piano, editing of the medical school alumni newspaper ----. My mother had long thought that the medical school of Tokyo University had no lectures in the morning, since I rarely attended morning classes. During the last three months of the medical school, I passed all final exams of clinical subjects by cramming one subject into my brain with amazing mental concentration, then, throwing out as much as I could of what I had just learnt since the drawer of my brain had limited capacity, and then cramming everything of the next subject. Still I managed to pass the national exam for the medical licensure in Japan and also passed the ECFMG (Educational Council for Foreign Medical Graduates) exam required for engaging in patient care activities in the United States. During 1959, I was a rotating intern at the US Air Force Hospital in Tachikawa outside of Tokyo. This was because I wanted to acquire sufficient clinical experience even though my ultimate aim was medical research and not patient care. I did not have a clear idea or wish to go abroad for further studies at that time. However, there is no denying that idea of going to the United States after the internship was acquiring some sense of reality as I was working in the environment of an American hospital with physicians who were also directly imported from the United States.

One afternoon, I took off from my duty as an intern and visited Prof. Hirotsugu Shiraki in his office at the Brain Research Institute of Tokyo University. He was a neuropathologist who first described post-anti-rabies vaccine encephalomyelitis and pointed out its similarity to multiple sclerosis. His report initiated a rush of subsequent EAE studies in the world. I had known Prof. Shiraki well because he was fond of mountain climbing and I, as a member of the student Alpine Club of the medical school, had often went to beg him for money, for example, “to buy a new tent”. I did not
realize then that the day would become pivotal in my life. I asked him for advice about the possibility of going to the United States immediately after my internship. His advice was clear, “Don’t go if you just want to go to the United States. Go if and only if you get accepted by a place really worth going for your future. I give you just an example of such a place. There is a new medical school in New York, called Albert Einstein College of Medicine. A guy with the name of Saul Korey, whom I have never met, is the first neurology professor there. He is trying to approach diseases of the nervous system from new angles by integrating basic science, clinical neurology and neuropathology, utilizing new basic physical and chemical technologies. If you manage to go to such a place, by all means you should go”. He showed me a just-published paper on a neutron-activation analysis of patient brains as an example. On my way back, I stopped by at a medical book store, Nankodo, on the street just outside of the medical school. There, by pure chance, I found two books edited by Saul Korey. One of them, “Neurochemistry”, had been published in 1956. The other, “Biology of Myelin”, had just been published (1, 2). I perused through them but subjects were mostly of basic science way beyond the poor intern who had just graduated from the medical school thanks to his skill to cram in a lot of information in a short time. I knew well the words of Ogai Mori, one of the major literary figures in the Meiji-Taisho era, “Blind respect is not a respect even if it is directed to an object worthy of respect.” That I had conveniently forgotten those words at that particular moment helped me into my subsequent career. My blind respect told me, “If I can go to his department at Albert Einstein, may be I can kill two birds with one stone and learn both clinical neurology and biochemical research of the brain”.

I immediately wrote to Saul. After introducing myself, I said “My ultimate aim is neurochemistry but I would like to learn clinical neurology as an essential background for my research career. Would you consider me as a candidate for your residency program?” This was my first contact with Saul. This was obviously reckless. Considering the mass of job inquiries I used to receive from all over the world, particularly from developing counties, no answer or, at best, a flat rejection would have been expected. It took a long time for letters to cross the Pacific those days. Nearly two months later, Saul did answer my letter without rejecting me outright. He said, “We’ll gladly consider you for position of Assistant Resident. Please come to the United States for interview”. My immediate reaction was, “Don’t be ridiculous”. It was half a century ago. Japan was still recovering from the war. The US dollar was at 360 Yen (now 90 Yen in October, 2009), and $500 was the maximum one was allowed to take out of Japan. Personal travels outside of Japan were literally inconceivable. I wrote back, “It is unrealistic for me to make a trip to the United States without any assurance of the position”. The next answer from Saul said, “OK, collect copies of your medical school records, the ECFMG certificate, and any letters of reference from whomever you can get and send them over.” Now this was realistic. I collected recommendation letters from Dr. Shiraki, Dr. Tomizo Yoshida (of the Yoshida sarcoma fame) who was then the Dean of the Faculty of Medicine, Tokyo University, and also letters from physicians at the USAF hospital where I was an intern to assure that I had sufficient English to function as a doctor in the United States. Then, Saul’s next letter said he would take me as an assistant resident from July 1, 1960. To this day I think that both sides were awfully brave, if not reckless. I knew nothing about Saul as a person, nothing about the environment of the school, and very little about his residency program. Saul decided to take me only on the basis of written records and letters without ever seeing me in person or speaking to me directly even over the phone. I realize that he could simply fire me after one year if I turned out to be useless as a resident. Nevertheless, it must have been a gamble on Saul’s mind that he accepted me as the first year resident without seeing my face. At that point, I told my mother, “I have been accepted by a hospital in New York. I will go to New York in the summer”. My mother being my mother, she hit me with a question, “Who is going to pay for the trip?” I was shocked into action and promptly applied for the Fulbright scholarship. Luckily, I was granted the travel scholarship of the Fulbright Exchange Program, which enabled me to make the trip to New York.

When I finished my internship, I became a staff member of the Department of Neuropsychiatry of the
Faculty of Medicine, Tokyo University, following Dr. Shiraki’s advice that I should join a department even though I would stay for a very short period of time. After only two and a half months in the department, I set sail on the President Cleveland from the rain-soaked Yokohama Harbor in mid-June, 1960. Mr. Godo Nakanishi, the founder of the Japan Wild Bird Association (Yacho-no-kai, an equivalent of the Audubon Society in the US) came to see me off because I was on the Executive Committee of the Association during my undergraduate and medical school years (Fig. 1).

Japan was then in the middle of a social upheaval. The new US-Japan Mutual Defense Treaty was the target of vehement protests not only of the far left but also of the moderate left including socialists. Huge demonstrations were staged nearly every day. I still clearly remember the radio news I heard next morning on the ship that Michiko Kamba, a Tokyo University co-ed, was crushed to death during the demonstration in the previous evening. The next two weeks were a dead bore. While the upper deck had a pool and other entertainment facilities, we, the poor students on scholarship, were housed in the lowest level of the ship with stacked beds. During the day, the scenery was the most monotonous ocean. We killed time playing ping-pong on the deck cursing every time when a mishit ball sailed over the edge of the deck into the ocean. Then, we had to buy another ball from the shop. I also spent time photographing albatrosses and red-tailed tropical birds that followed the ship. I still have slides of those birds. I was never really seasick but was chronically uncomfortable with a mild sense of motion sickness throughout the voyage. The trip was interrupted by a half-day stopover at Honolulu before it arrived at San Francisco. I watched with awe as our ship passed under the Oakland Bay Bridge. Luckily, the first jetliner services between the west and east coasts of the United States had started a year earlier and I was flown from San Francisco to the then Idlewild (now JF Kennedy) Airport in New York overnight. Many of my contemporaries who went to the US those days crossed the US continent to the east coast by train taking additional several more days. Thus, I arrived at the Einstein/Bronx Municipal Hospital Center one week before I was to start my duties as a first-year resident. A shared room was assigned to me at the Staff House on the hospital ground.

Figure 1. Mr. Godo Nakanishi, the founder of the Japan Wild Bird Association, kindly came to see me off as I sailed off from the Yokohama harbor. The man in the dark suit is Mr. Tokumi, also a member of the committee. (Translation of the original caption written by Mr. Nakanishi: I and Mr. Tokumi went to the...
Yokohama harbor to see off Mr. Suzuki, a member of the executive committee of the Japan Wild Bird Association (center) who went to study in the US. Mr. Tokumi presented Mr. Suzuki with a fancy key chain (what for, I don’t know). The ship in the background is an ocean liner that carried Mr. Suzuki.) (published in “Yacho” (=Wild Birds) in 1964)

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**Life as a Neurology Resident**

My first encounter with Saul was during the introduction of new residents in the conference room of the Department of Medicine in the Jacobi hospital, one of the two major hospital buildings on the campus of the Bronx Municipal Hospital Center. Neurology was a section of the Department of Medicine at that time. Dr. Irving London, the first Chair of the Department of Medicine, first gave an introductory remark and then turned around and said, “Saul, anything you want to say?” A big guy sitting close to him just shook his head with his mouth tightly shut and did not utter a single word. My first impression of Saul was not a very favorable one. He appeared to me arrogant and brusque (Fig. 2). However, Saul was in a totally different mood next day at a meeting of only Neurology residents. He was congenial and explained everything in detail to us, the newly arrived residents. I learnt later that the section of Neurology was to become an independent Department of Neurology soon. Saul may well have felt at the meeting of the Department of Medicine, “I will soon be running my own show”. I had known that the AECOM was a newly established medical school but did not realize until new residents got together that at least three of my fellow Neurology residents in the same year were the first AECOM graduates – Joan Rumberg, Lenny Green and Cal Ackerman (my memory is not clear; was Carl Rosengart also in the first class of Einstein?). This meant that the AECOM admitted its first students four years earlier.

![Figure 2](image-url)

**Figure 2**: Saul and his signature.

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Albert Einstein College of Medicine was founded from the beginning with a contract with New York City that the city built a new Bronx Municipal Hospital Center on the adjacent ground as its teaching hospital. Thus, residents were actually New York City employees and the annual salary was $2200. At less than $200 per month, residents’ life was not luxurious even in 1960 to say the least. Nevertheless, nobody complained, at least openly, because it was the time when interns in some of the most prestigious hospitals, such as the Massachusetts General Hospital, worked without pay. We residents were provided with a room shared with another resident in the Staff House on the hospital ground, and meals at the hospital cafeteria were all free including night meals while on night duty. Even family members of residents could eat at the cafeteria free when accompanied by the residents. Those nights when the hospital cafeteria served steaks were particularly popular among residents’ families. Those days, first-year residents took night calls every other day and every other weekend on busy services, such as neurosurgery. You were rarely able to sneak some sleep during night duties. Particularly when I was on duty for a weekend, my duty started when I reported to the ward Saturday morning and continued for two nights and three days straight until I went off duty in late afternoon of Monday. Under these working conditions, my resident life was 100% devoted to patient care during the first two years even though I had come all the way to New York looking forward to be trained in medical research.

For two years I had opportunities to observe Saul as a clinical neurologist before I entered the research laboratory. Several fond memories come to my mind from that period. I arrived in New York in the summer of 1960, which was the year of the Kennedy-Nixon Presidential election. I was deeply impressed by the American political environment by watching the first series of TV debates between the candidates. Saul was then driving a bright red Saab equipped with a three-cylinder engine, which required not just gasoline but a mixture of gasoline and oil as its fuel. It was a \textit{rara avis} and students nicknamed it, “Koreymobile”. On its bumper was a big banner, “Kennedy for President”. The American political far left was and still is not far from the moderate center for the rest of the world politics. Within this context, the Jewish population with its relatively high concentration of intellectuals, artists, scientists tended to be on the left side of the American political spectrum and the Einstein faculty was no exception.

One day during my first year residency, a young woman was admitted to the ward from the emergency room with a text-book history of tetanus. She had stepped on a rusty nail a while ago and developed troubles with her jaw movements that day. As soon as Saul heard about the patient, he gathered all residents on the ward and declared, “Tetanus can be cured completely. Given proper care, there is no reason for any tetanus patients to die. I won’t tolerate it if you let any tetanus patients die on my service.” From that day, residents on night duties slept on the bed across the room where the patient bed was. One night when I was on call, a nurse ran to me, “That patient pulled out the tracheal tube herself!!!” When I rushed to her bed, she was already a little cyanotic. I tried but, in panic, the tube would not go back in smoothly. It must have been a matter of seconds, but I felt it like eternity until the tube was finally inserted back and the patient started breathing normally again. What a relief!! Thus, I avoided Saul’s wrath, and the patient recovered completely and was discharged. Throughout this episode, Saul stopped by at the ward every day, examining the patient and checking her chart. I learnt an important lesson from Saul, the clinician. There is a follow-up story about this episode. The patient’s husband was apparently a cab driver. A few months after the patient was discharged, my wife had an occasion to take a taxi home. As it was passing by the Jacobi Hospital, the driver told my wife, “Recently, my wife contracted tetanus and was taken care of in this hospital by the neurology people. Everybody was wonderful and she received the best care. She is completely recovered and now back home. This is the best hospital in the world.” When my wife told me this story, I couldn’t help but wonder, “What if it had taken a little longer to insert the tracheal tube back in??”

During the first three months of my neurology residency, I rotated to neurosurgery as a part of the training program. I had thought I knew the American hospital system from my experience at the
USAF Hospital Tachikawa during my internship. However, my daily life in the neurosurgery service was a revelation. The Bronx Municipal Hospital Center is in the Bronx, the northern part of the New York City. It is the only part of the New York City that is on the North American continent. All other parts are on islands. The Bronx, particularly its southern part, became notorious a decade later as a very dangerous place with poverty and crimes, but it was still a quiet residential area around the AECOM in the early 1960’s. But, on the neurosurgery service, I saw patients of all types, -- a young girl who was shot in the head at night, a young guy who jumped into the pool from a high tree branch trying to show off to his girlfriend and ended up breaking his neck, ---- *ad infinitum*. First year residents had no time whatsoever even to sit except while eating meals or, when you were not on call, between 6:00 pm to 7:00 am next morning. When I visited fellow resident friends in pathology, they were sitting at their own desks!! Pathology was located in the basement of the hospital, but I thought up and down was mixed up and they were in the heaven and I was in the hell.

I still remember a fellow first-year resident, Zuckerman (I do not remember his first name), who was also a “rotater” to neurosurgery from general surgery. He claimed, “I am a devout Jewish. According to the Jewish rules, I cannot work from the sunset on Friday to the sunset on Saturday. I have to ask you to take calls during those periods. I will take calls every Sunday”. I didn’t think it was a good deal for me, but I accepted for a while since it is always difficult, if not impossible, to deal with anyone who likes to prop up god and hide behind it. But soon it was discovered that, even according to the Jewish rules, one was allowed to work during the Sabbath if it was a matter of life and death. Zuckerman had to give up nice Friday evenings and take calls. But the story was not that simple. He reluctantly stayed in his room in the Staff House in Friday evenings. Since he was in the neurosurgery service, he often got calls after midnight. The Jewish rules dictate that one cannot use any contraption that is a product of human civilization (if I am not mistaken, there were no flights in and out of Tel Aviv airport from the sunset Friday to the sunset Saturday for many years). He therefore would not pick up the phone in his room. Someone had to go from the hospital to his room to wake him up and summon him to the operating room. As often is the case in many hospitals, the OR of the Jacobi Hospital was on the top floor. Zuckerman, not being allowed to use that epitome of civilization, the elevator, ran up the stairs to the operating room. Needless to say, he was totally useless for some time panting and exhausted. I firmly believe that religion is at the bottom of most, if not all, human ills and that true peace will never come on the earth as long as plural monotheistic religions exist. This time in 1960, I could not avoid being directly and personally victimized by a religion, or more accurately, by people who proclaim to be religious.

There was another hilarious incidence concerning the Jewish rules. One day, an elderly patient was admitted with a mild stroke. In a few days he was doing quite well, so I told him that I would put him on regular diet. Unexpectedly, I encountered a strong resistance. He kept insisting that he must have **** diet, which I had never heard of. After several exchanges of futile arguments, I went back to the nurses’ station, “That patient is well enough to be on regular diet but he is insisting that he must have a strange diet that sounds like “kosher” diet. What is it?” The room was immediately filled with loud laughter. I for one was totally at a loss having no idea why I was being laughed at. According to the concept common in Japan, I had thought Jewish was defined as a race and did not know that it was defined by a religion. Naturally, I had no idea whatsoever that it imposes so many strict rules on people’s life. Zuckerman’s case above was one example, and this story about the kosher diet was another. This alone would keep me away from the Jewish religion, because I love shrimps, oysters, pork, particularly bacon and eggs with my toast in the morning. These incidences did not diminish my life-long antipathy against all organized religions.

The Albert Einstein College of Medicine, itself being a unit of the Yeshiva University, the bastion of the Jewish religion, was and I assume still is supposed to follow the Jewish rules. For example, having a class that required attendance by students was prohibited from Friday evenings to Saturdays. The meat and dairy days were strictly separated at the college cafeteria. Not only the days were
separate, the trays, dishes and utensils were also separate. To push it to an absurdity in my mind, separate openings existed where finished trays, etc were placed for washing. If you bought a chocolate bar from a vending machine during Jewish holy days, it came out with a sticker proclaiming that it was blessed by a rabbi for consumption during the Sabbath. My wife joined me from Japan in December, 1960 and we rented a basement apartment of a private house just adjacent to the hospital ground. The landlord who was not Jewish told us the story. Before us, two Einstein students lived there. They were devout Jewish. They turned on all electric switches before sunset Fridays and kept them on until the sun went down on Saturdays. I guess it is true that electric switches are products of human civilization. Under these circumstances, it was no surprise that the Yeshiva University side complained often that Einstein faculty regularly worked Friday evenings and on Saturdays. Luckily to me, these complaints were completely ignored by the Einstein faculty members.

It was during my residency period when I realized that American education system was quite different from that of Japan. One day we residents were discussing something, -- I no longer remember the subject. The discussion came to the point that something was “close to infinity but not quite”. One of my fellow residents said, “Then it is infinity minus one”. I, as someone who always loved “useless” mathematics since my college student days, was appalled and protested, “There is no such mathematics”. It was obvious, however, that it would have made no difference in the discussion if I had argued in Japanese. If I had said, “There are many sizes of infinities and in fact, there are an infinite number of infinities of different sizes. Whether sizes exist in between different sizes of infinities was one of the biggest problems in mathematics until the establishment of Kurt Gödel’s logical undecidability principle.”, I am sure I would have been suspected of having come not from the Mars but from the Pluto. Another similar but much later example; one of my fellow faculty members came to borrow an electronic calculator from me saying that he had to do some logarithmic calculations. I handed him my calculator and told him that he had to use the \( \log \) key if he needed to do base 10 log calculations and the \( \ln \) key for natural log calculations. I couldn’t believe my ears when he replied that he had never heard of logarithm other than base 10. I told him that one could not get in to college and major any branch of science in Japan, if one did not know the natural log. His reply was, “Why should I know such a totally useless thing?” I then realized anew that the United States is by far the most pragmatic country in the history of mankind. There is an indomitable undecurrent among the general population, “What is useless cannot be valuable”. Because of this, even scientists who are not interested in practical applications of their work are literally forced to come up with some justification that their work, although its usefulness may not be obvious now, would one day be proven useful for mankind. Otherwise they may lose their research funding. To my mind, they are selling their soul to Mephistopheles in order to catch Gretchen. This extreme pragmatism of the US intellectual climate is entirely contrary to my ingrained conviction through my upbringing and education. To me the scale of practical usefulness and the scale of value are two separate and mutually independent parameters. This, together with the unreasonably strong religion, was the major factor that made me to conclude that the US, despite so many advantages while I was actively working, is not the country I wanted to live after my active professional life was over. It was this psychological factor that prevented me from acquiring the US citizenship while living in the US for altogether 47 years. I am now back in Japan and have given up my US residency status. I have crossed the Rubicon at this old age and I have no regrets.

**Saul and Einstein Environment**

Before I present my fond memories of my life in the laboratory with Saul, I would like to give an objective description of the professional environment that surrounded Saul. When the Einstein College of Medicine was founded in the middle of the 1950’s, discrimination against Jews had not yet been completely erased. Saul himself graduated from the Medical School of the University of Western Ontario located in London, Ontario, Canada. During one of the long evenings in the lab with me, he told me that no medical schools in the United States would accept him as a student. I understood that the AECOM had been created as a college of the Yeshiva University, the bastion of
Jewish education, to combat against this anti-Semitic atmosphere. Albert Einstein who was still alive blessed its inauguration by allowing use of his name. The first students were admitted in 1956. The initial faculty members were all Jewish recruited from among the most promising young Jews not only from the US but also from many corners of the world. Among them were the husband and wife team of Ernst and Bertha Scharrer of the neurosecretion fame (Anatomy), Alex Novikoff who later provided the morphological base for the biochemical concept of the lysosome proposed by Christian DeDuve (Pathology), Alfred Gilman who was known for his pharmacology textbook with Goodman and is also the father of Alfred G. Gilman who later received Nobel Prize for his discovery of G protein together with Martin Rodbell (Pharmacology), Leo Davidoff who was one of the top disciples of Harvey Cushing (Neurosurgery), Herbert Scheinberg who was known for his work on Wilson disease (Medicine), Abraham White who was also famous with his biochemistry textbook (Biochemistry). The college was developing with an amazing speed and vitality for a new medical school. We should remember that the political climate in the United States was in the dark ages of its short history during the 1950’s. It was the time when Joe McCarthy campaigned in the US Congress against any hint of communism, in fact, also socialism, since he could not distinguish the communism from socialism as the majority of the US population still cannot. His hysterical “red purge” was rampant and many talents in all fields of intellectual endeavors and the art world were banished with the label of “RED”, literally a “scarlet letter”. They suffered from irreparable damage not only to their reputation but also to their daily lives, since many lost their jobs and many potential employers would not hire them. This was precisely a mirror image of the Zhdanov doctrine under Stalin in the Soviet Union, and the negative consequences were the same. I do believe that the AECOM should be given a great credit because it courageously hired many of such young talented people when many coward universities shied away from them in order to “protect” themselves. Alex Novikoff was one of those people literally rescued by the AECOM. I am not without complaints, in fact I do have a lot of complaints, against the Einstein administration in later years, but I do respect the courage it demonstrated in its early days to fight against the prevailing evil wind. Saul Korey was invited to such an environment as the first Chief of Neurology and soon the first Chairman of Department of Neurology. He received his neurology residency at Columbia University. He had also spent time in the laboratories of some of the most distinguished basic scientists, such as David Nachmansohn, one of the earliest researchers who studied acetylcholine, Harry Grundfest, a physiologist, and Severo Ochoa, a Nobel laureate. Saul had had publications from his work in these laboratories. Thanks to his background in basic science laboratories, Saul was able to understand science on its own sake independently from any possible applications to clinical medicine or to human disease. As a person, he was gregarious, aggressive and argued vociferously pushing his own ideas like a bulldozer. This was not necessarily a trait that would endear him to everyone. He had a lot of supporters but also a lot of detractors, with relatively few in the middle neutral position. Gil Glaser, who was chairman of Neurology at Yale in later years, once told me long after Saul’s death, “I was the Chief resident in neurology at Columbia when Saul was a resident. I believe I was the last person on the earth who could give orders to Saul”. I don’t doubt that Gil must have been right.

**Initiation to the Korey Lab**

After two years of residency, I was summoned by Saul, “You came with the goal of gaining experience in the research lab. From the third year, you should limit your clinical duties to night and weekend calls and start working in the lab.” The main subject of the Korey lab then was Tay-Sachs disease. This is a rapidly fatal genetic neurological disorder of infants. Patients are born apparently normal, but first symptoms and signs appear around six months. Clinical manifestations are largely limited to the nervous system. After a relentlessly progressive clinical course, most patients die by 3-4 years. It is highly prevalent in the Ashkenazi Jewish population, so much so that for many years, it was thought to occur exclusively among Jews. From the mid-1930’s to the early 1940’s, Ernst Klenk identified a new group of lipids that accumulated abnormally in patients’ brain and named it “ganglioside”. When I arrived in the Bronx, Terry and Korey had just discovered that those distended neurons in the brain of Tay-Sachs patients contained abnormal
organelles with an onion-like membranous structure (3). They called them “membranous cytoplasmic bodies (MCB).” Some French authors still call them “Terry bodies.” Soon after I entered Saul’s laboratory, Makita and Yamakawa (4) determined the chemical structure of the ganglioside in Tay-Sachs brain. It is now called GM2-ganglioside according to the most widely used nomenclature by Svennerholm (5). However, its biosynthesis and degradation, and naturally the mechanism of its abnormal accumulation in Tay-Sachs disease were a complete mystery in the early 1960’s. Saul was trying to approach the problem by integrating clinical medicine, pathology, electron microscopy, and analytical and metabolic biochemistry utilizing less than 1 g of brain tissue obtained by brain biopsy. This was epoch-making. The first set of the results of this team effort was published in 1963 as a massive 104-page article (6). When its reprints arrived, Saul gave me a copy to which he inscribed, “To Kuni whose success is certain.” (Fig. 3). He must have thought, “This young Japanese came all the way from Japan and is struggling in the lab. He needs a bit of encouragement.” This trick worked and I was happily working day and night in the lab. I was first given the task of measuring oxygen consumption of biopsied brain slices under various metabolic conditions. By a pure coincidence, I used the Warburg manometer identical with the type I used in Prof. Kimura’s laboratory several years earlier as an undergraduate student. But the genetic diseases, such as Tay-Sachs disease, are rare, and brain biopsies from patients were on the average no more frequent than once every few months. I was therefore also given another project to do during intervening periods. This was to examine protein synthesis in vitro using isolated microsomes. Although Saul’s long-range plan was to apply the system to biopsied brain tissue from patients, I first tried to establish the experimental system using rat brain. Protein synthesis was measured by incubating the brain microsomal and cytosolic fractions prepared by ultracentrifugation, together with radiolabelled lysine. The system was then scaled down so that it could be applied to a small portion of already tiny biopsied brain tissues. This series of studies resulted in an article which, for the first time in my life, I could really call “my own work” (7).

Once in the laboratory, it was immediately obvious that this was the life I wanted. Either taking care of patients or in the lab, I was working until late into the evening every day and I did not mind that at all. However, in clinical medicine, a clinician’s time is not his but his patients’. It was impossible to plan anything ahead of time. As a third-year resident, I had no patients on the ward and was taking only night calls. I had to go to the hospital only when I was needed. Nevertheless, it was totally unpredictable as to when I might get a call. Since I could not interrupt an experiment in the middle and go to see patients, I had to stop working in the lab at 5:00 pm on the day when I was on duty. In some nights I might be busy getting multiple calls, but in some other nights, I might not get any calls at all. Then, I felt, “I could have done this and that in the lab, if not on call.” Even during daytime when I was supposed to be free from any clinical responsibility, I had to talk to patients’ families when they telephoned for any reason. It was not the long hours but the mental difficulty of frequently switching back and forth between patient care and lab work that eventually took me out of clinical neurology altogether. I do have the medical license in Japan and also in New York State. Legally, I can practice medicine or surgery tomorrow. But, to do so now would endanger not only patients and the society but also myself. During later years in New York, the only tangible benefits of my MD license were limited to the occasional privileges accorded to licensed physicians such as escaping from minor traffic infractions or declining jury duties. Some of my friends who remember my old days say, “You used to be a neurologist.” Many other colleagues who got to know me more recently do not even know I am a licensed physician and in fact was once engaged in patient care activities. Frequently I receive correspondence addressed to me as a Ph.D.
Looking back from far away, both in time and distance, I learnt a lot from Saul. Like any academic clinicians in Japan who divide their time between patient care and laboratory activities, he was shaking test tubes and running chromatographic columns himself in the evenings and during weekends (Fig. 4). I did not think anything of it after coming from Japan but I realized later how extraordinary it was for an American clinician. He carried back and forth between home and the laboratory his huge square leather bag, the kind salesmen carried, packed with documents and literatures. One Monday morning, I was busily preparing for the experiments I had planned for the week. I was not entirely happy when Saul caught me and explained to me in detail about the new pathway for bacterial cell wall lipopolysaccharide synthesis, which he had read about during the weekend. I now understand well that he wanted and even needed someone to talk with in the lab while working during the evenings and weekends. He had two technicians working for him but they would not work in the evening or weekends. While many researchers worked in the lab in the evening, I was the closest to Saul physically since my bench was opposite from Saul’s in the same room. We kept discussing all kinds of subjects into late evenings, from purely technical laboratory problems, fundamentals of science, arts, politics and social issues. He was the type who loved the challenge when people disagreed and argued against him. He became unhappy on rare occasions when I kept agreeing with him. He wanted to be challenged by counter-arguments. And I must say that suited me fine too. I do remember some of the things he said in such occasions. For example, when Nick Gonatas was to go to Penn, he said to me, “If you have someone good, you must find a good opportunity somewhere else for his future, even though losing the person may mean a big loss to yourself.” On another occasion, “The only experiment worth doing is the one done right. If you have to make excuses for no money, no time, no manpower, or no equipment, then you might as well not do the experiment. You are wasting your time.”
New York Musical Scenes
Lest the above may give a wrong impression, I should say I did not work every night in the lab. When I arrived in New York in 1960, it was the last season of Charles Munch at the helm of the Boston Symphony. In addition to its regular season series in Boston, the Boston Symphony had a series of 6 or 8 concerts in New York during the season. I bought the season ticket for the Boston series. It was also the last season for the Boston Symphony in the Carnegie Hall, which had just been rescued from the wrecking ball by concerted efforts of musicians and citizens, such as Isaac Stern. Also, since I did and still do have strong affinity to contemporary music, I was going to the series of contemporary music concerts held monthly in the Carnegie Recital Hall. The series was basically for performance of new compositions by young, active American composers, such as Ralph Shapey, Charles Wuorinen, Milton Babbitt, Mario Davidovsky, Harvey and Sophie Sollsberger, et al. It was well before the time when Wuorinen had his bitter tenure fight against the music department of Columbia University. The reason I bring up this series is that I experienced an unforgettable evening in one concert. Each of the concerts included one “contemporary” piece which had already established itself as a classic in addition to new compositions. In one evening, they played Edgar Varèse’ “Ionisation”. And Varèse was in attendance!! At the end of the performance, he stood up from just a few rows in front of me, turned around and acknowledged the applause. The Carnegie Recital Hall is tiny. He was literally face to face with me. He was a big man with a rugged face. His face and his demeanor are etched into my memory forever. Varèse died within a year or two afterwards. In that series, I often saw Dr. Ryuta Ito, who was a few years senior to me as an alumnus of Tokyo University Faculty of Medicine. He was also known in Japan as an active composer in addition to be a physician. I believe he was later Professor of Pharmacology in Toho University School of Medicine in Tokyo. I remember he once made a point to me during the intermission in one of the concerts that the main issue in contemporary music was how to “clash”
different sounds. His use of the word, “clash” somehow made a long-lasting impression in my mind. Another talented young Japanese composer, Toshi Ichiyanagi, was studying then at Julliard. He lived near Amsterdam Avenue close to Columbia University. We, several of the Japanese residents at the Bronx Municipal Hospital Center, often played mahjong with him. If my memory is correct, he had just come to New York after a triumphant season a few years earlier when he swept the NHK competition winning the first prizes in all three categories of compositions, solo, chamber, and orchestral. He also received the Suntory Music Prize in 2002. Seiji Ozawa also had made his dramatic debut around the same time replacing Leonard Bernstein at the last moment in a Tanglewood concert. But, I did not have a chance to listen to him until much later.

When I told Saul that I was not working in the evening because I had a concert to go, Saul made a long face. It meant to him absence of the opponent in the evening arguments. In Japan, I often hear strange stories that departmental staff cannot go home until Professor goes home. Luckily to me, it was New York. No matter how long a face Saul made, I just ignored it and enjoyed the musical life in New York.

Saul’s Research Philosophy and his Staff

Saul’s laboratory at that time was unique. In the research group led by Saul, he had been the only clinician until I joined the group. He often told me during our late evening discussion, “This lab does not need any more clinicians beyond I and you. We need rigorously trained basic scientists in several key areas”. The corner of the first floor of the Forchheimer building was teeming with top-class basic scientists, who later established themselves in their own fields. Among them were Bill Norton, who was recognized for his works on neural cell isolation and on myelin and who later was President of the American Society for Neurochemistry and Chief Editor of the Journal of Neurochemistry, and Bob Ledeen, who joined the Korey laboratory to participate in the Tay-Sachs disease project and devoted his entire research career to studies of gangliosides. Both Bill and Bob were organic chemists by training. Next door to the Korey lab was the neuropathology laboratory headed by Bob Terry, who was an indispensible collaborator of Saul from the beginning, and Nick Gonatas, a young upcoming neuropathologist, who later moved to the University of Pennsylvania. Both Bob Terry and Nick had been trained by the godfather of neuropathology, Harry Zimmerman, at Montefiore Hospital in the Bronx and were both expert electron microscopists. Nick’s wife, Jackie Gonatas, had been Saul’s technician as Jackie Orloff. My wife, Kinuko, was being trained by Zimmerman when I entered the Korey lab. It was after Saul’s death when she joined Bob Terry’s group. In Biochemistry department a few floors above was Maurice Rapport, who is one of the pioneers in the field of glycolipids. He had discovered lactosylceramide (he named it cytolipin H). Maurice often came down to our floor and socialized with us. I never forget what he told me one night when I was alone in the lab with him, “Your work is not finished until you publish it.” Bill Norton and Bob Ledeen remain good friends of mine ever since. Both are three years older than I. Given my feeble knowledge of organic chemistry, Bill has been of great help for me. He has an unusually lucid, logical mind. There have been even a few Nobel laureates who did not give me an impression of being particularly intelligent when we discussed scientific matters personally. But I count Bill as one of the most intelligent people I have met. Bob Ledeen is a solid organic chemist who accomplishes a lot by quietly working in the lab. Bill retired a few years ahead of me, but Bob is still active. Looking back, those were happy years. We just worked together in the lab until late at night only pursuing our research interests without any administrative burdens.
Figure 5: At the softball-barbecue party in Saul’s house in late spring of 1963. The ladies are Mrs. Korey, Doris, (left), and one of his daughters (right). Saul was complaining bitterly about his low back pain while playing softball. In retrospect, it must have been a symptom of his cancer that killed him four months later.

We all lost Saul

We all happily drove ourselves busy in the Korey lab. However, this happy state was not to last long. One day in May or June of 1963, Saul held a house party for residents and young attendings. We played softball and barbecued on his lawn (Fig. 5). Saul was complaining about his back pain while playing softball. In retrospect, that must have been the tell-tale symptom of his cancer. Apparently, he was deceived because he had long suffered from back pain and thus did not pay enough attention he should have paid. Soon afterwards during the summer, he suddenly developed an intestinal obstruction and was diagnosed as having pancreatic cancer. Laparotomy indicated extensive metastases to the liver and no further surgery was possible. Saul died only three months later. There are conflicting reports about the nature of his tumor whether it was pancreatic or intestinal. I do not know its true nature. However, the Neurology Department put up the last fight against the challenge. When Saul’s illness was diagnosed as an inoperable cancer, an article published in Science just earlier came to our attention. It was authored by Albert Szent Gyorgi, who had won the Noble Prize for his discovery of vitamin C. It described a potent anti-cancer agent extractable from human urine. I do not remember the name Szent-Gyorgi gave to the agent. We promptly placed a large glass jar in every men’s room throughout the hospital and the medical college and collected them every day. Bill Norton and Stan Samuels drove to Woods Hole to learn directly from Szent-Gyorgi how we should go about preparing his anti-cancer substance from collected urine. None of us were optimistic that it would cure a cancer declared by surgeons as inoperable. We all knew too well that we were trying to hold on to a piece of straw as we were drowning. Still we felt that we could not accept defeat without putting up a fight. I remember well Maurice Rapport’s words about Szent-Gyorgi’s anti-cancer substance, “We don’t want to see Saul die as the last person who had to die of cancer.” None of us did anything-else for two months other than collecting and extracting urine for the elusive anti-cancer substance. In the eyes of bureaucrats,
this would have been viewed as an inexcusable dereliction of our duties for which we had been hired. But, I would say without hesitation, “The real life cannot and should not be measured by ready-made rulers only”.

Saul left us seemingly in an instant. Dying in the middle of his 40’s, he did not have enough time to make lasting contributions of his own. Few even remember his name now. Some even say he accomplished nothing. However, my interactions with Saul, short as it was, gave me the base on which I could shape my career in later years. More than anything else, it was his vision as to which direction academic neurology should be heading that guided me. Bill Norton agrees with my assessment of Saul’s influence. At the time of his death, Saul was working on his concept of the “gangliosidase system” (8), meaning that there should be a metabolic system that degrades gangliosides systematically and that something must be wrong somewhere in the system in Tay-Sachs disease. It foresaw the identification of the enzymatic defects in lysosomal diseases, cloning of the responsible genes, identification of disease-causing mutations, and the currently active search for effective treatments, all of which occurred after Saul’s death.

If Saul had not died when he died, I probably would have returned to Japan within a few years. After Saul’s death, I was asked by the senior members of the department just to continue what I had been doing with Saul. I groped around and slowly learnt how to swim myself. Then it was inertia that defined my subsequent path. I ended up living and working in the United States altogether for 47 years without ever making a conscious decision to remain in the US. I already mentioned above the reason why I decided to return to Japan permanently after my retirement from active academic life. That I could not stand watching the smirk expression of George W. Bush on the television screen gave me the last and definitive push on my back to come back to Japan. Looking back, I feel that, after all, I just followed the path Saul had shown me. I was given an opportunity to give a Saul R. Korey Memorial Lecture at the annual meeting of the American Association of Neuropathologists in 1993. I would like to end this reminiscence by quoting my concluding paragraph at the end of the published lecture since it still expresses well how I feel about Saul.

“I am writing this exactly 30 years to the month after Saul's death. Few remember Saul's work. He simply did not have time to make long-lasting contributions of his own. Nevertheless, those of us who had the privilege to know Saul and work with him realize too well that he anticipated exactly where the field should be moving. He set his own laboratory in motion in that direction. He knew that the "useless" science driven by inner curiosity of basic scientists is the most useful in the long run for solving more pragmatic problems of the clinically oriented. I still vividly remember one Monday morning when Saul caught me -- he needed someone, anyone, who might listen -- and discussed with great excitement a paper on the bacterial cell wall lipopolysaccharide synthesis which he had read during the weekend. If not his own work, it was his vision that set him apart from other "competent" scientists. Most of the conceptually modern developments of Tay-Sachs disease occurred after his death. Yet, I cannot help but to feel that Saul would smile and say, "I knew it", if he were to see what has happened in the past 30 years.”

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