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From Tryptophan to Hydroxytryptophan: Reflections on a Busy Life

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Abstract

Given the very difficult odyssey of my early years, who could have imagined the incredible and successful journey that constituted my life path after age 13? I was born into a Jewish family in Breslau, Germany, right before the rise of Nazism and Hitler's election. After Kristallnacht, when my father was taken to Buchenwald Concentration Camp, we had to leave Germany as soon as possible. The first opportunity came in May of 1939, when we boarded the SS *St. Louis* bound for Havana, Cuba. Almost all passengers were denied entrance into Cuba, and the ship had to go back to Europe, where I ended up in France. In December of 1939, during World War II, I was fortunate to be able to leave France. This time I made it to Cuba, where my father was already in residence. A year later, my entire family was allowed into the United States. I took advantage of all the educational resources in this land of opportunity. I graduated valedictorian of my high school class and earned a four-year scholarship to Rutgers University, where I obtained a Bachelor of Science degree. I went on to earn a Master's degree from the University of Connecticut and finally a PhD from the University of Illinois. Within two months after graduating from Illinois, I was hired as an assistant professor of nutritional biochemistry at Rutgers, where I enjoyed a most productive research and teaching career. My PhD research involved tryptophan and niacin metabolism in the chick, and upon arrival at Rutgers I continued amino acid studies with the goal of assessing the essential amino acid requirements for egg production. This research was crowned with success and was followed with amino acid requirement studies for maintenance and for growth in rabbits, and ultimately with a reevaluation of requirements in adult humans. An outgrowth of the maintenance requirements led to a series of investigations into

the metabolism of histidine, histamine, and carnosine (a histidine-containing dipeptide). Histamine, we found, plays an important role in wound healing and stress management. Pyridoxal phosphate is the cofactor for the enzyme histidine decarboxylase required for histamine synthesis and similarly serves as a cofactor for hydroxytryptophan decarboxylase, the enzyme that is part of the pathway to serotonin synthesis. Investigations into these pathways led to interesting findings: brain concentrations of serotonin could be increased by supplementing the diet of rats with tryptophan and pyridoxine; the elevated brain serotonin levels had behavioral consequences. Alcohol craving, addiction, and withdrawal symptoms are affected by serotonin concentrations in the brain, and alleviation of these conditions can be achieved with simultaneous administration of serotonin and dopamine agonists. In the midst of our early amino acid studies, we serendipitously also became involved with lipid metabolism in relation to atherosclerosis and blood cholesterol in a chicken model. This work led to the recognition that soluble fibers, like pectin, had strong cholesterol-lowering properties that were beneficial in lowering the incidence of coronary plaque formation. The research success that I have enjoyed has been coupled with the gift of three accomplished children who are making important contributions as professionals in their fields of endeavor. My wife and I are also blessed with 10 wonderful grandchildren, our pride and joy!

FAMILY HISTORY

Family lore has it that at the precocious age of 2, in about 1930, I carried out my first memorable act that was to bring me fame: I grabbed my uncle's hat and tossed it out the window of his moving automobile. This uncle, who was visiting Breslau, died shortly thereafter, but I strenuously deny any responsibility!

Life began for me on March 4, 1928, in Breslau, Germany. My mother was also born in Breslau, and her mother, Emma Wund Gottheiner, was the second wife of my grandfather, Wolf Gottheiner. He came from a small town near Breslau, Kempen (now Kepno), which became Polish after World War I. I was told he was a furrier in his youth, but when I knew him, long after he had moved to Breslau, he was the owner of a shoe factory. His first wife, who died young, bore him four sons and a daughter. All four sons were killed at the Eastern Front fighting for the Kaiser during World War I. My wife and I saw their names inscribed on a stone monument to Jewish soldiers from Breslau who died in World War I. This monument is one of very few graves or monuments still standing in one of the two Jewish cemeteries in Breslau (now Wrocław), Poland (since the end of World War II). Both of my mother's parents died of starvation in 1943 in the Theresienstadt Concentration Camp in Czechoslovakia.

My father, George Fisher, was born in Kempen. Both his parents had lived in Kempen, where my grandfather Fisher operated a flour mill. My grandparents Fisher and their family moved to Breslau in 1912. In addition to my father there were two daughters. The older daughter, Nelly, married physician Kurt Jakubowski, who had a medical practice in Danzig. The German Nobel Prize-winning writer Guenter Grass mentions in his book *Cat and Mouse* that my uncle was his family physician. The younger daughter, Hilda, married a businessman named Hauschner, who died at a very young age, leaving a son, Ernst, who lives in Israel. In 1927, a year before I was born, my grandfather Fisher died in Breslau. My grandmother Fisher was with my other grandparents

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when they were transported to Theresienstadt, where she died of disease and starvation, as did my aunt, Hilda Hauschner.

I loved visiting my grandparents Gottheiner. My grandmother, who I later discovered was considered by others a very stern lady, showered me with love and attention. When I got older and could read, my grandmother, who had exemplary handwriting, would write my name into my books. I still cherish the few such volumes that survive.

My grandmother, I later learned, was also a very charitable person. She helped poor brides obtain a dowry (an important aspect of being able to get married in those days) and financially assisted widows and elderly people in the Jewish community at large. I remember a most touching incident when I was 5 or 6 years old. An elderly widow whom my grandmother had befriended came to our apartment for a friendly

visit with my mother. It was my birthday, and the lady saw some of my presents on a table. Before my mother could say anything, the visitor had turned around and left the apartment. She came back perhaps an hour later with a beautiful collection of little toy chicks with a mother hen in the lead glued to a pretty piece of cardboard. She had made the chicks and the hen from cotton, dyed yellow, and used toothpicks, wooden matches, and wire pipe cleaners to give the animals their shapes and features. Knowing from my mother how impoverished this widow was, her present gave me a stab in the heart. She wanted so badly to present me with a gift and so thoughtfully found something that she could make herself and that she could afford. I remember thanking her with tears in my eyes, and I have never forgotten this frail woman and this experience with poverty.

Both my parents, Johanna and George Fisher, received a higher education. My mother became a teacher, and my father, who attended several universities as was customary in Europe at the time, graduated from the University of Breslau with a doctor of law degree. Neither of my parents practiced their professions in Germany. My mother received a teacher's certificate again in the late 1940s in the United States and was a special education teacher in a South Jersey public school until her untimely death in a car accident in 1953. My father, after serving for four years in World War I, worked first for a pharmaceutical company in Koenigsberg, East Prussia, and after marrying my mother in 1927, in the shoe factory of my grandfather Gottheiner.

GERMANY BEFORE WORLD WAR II

Although I was only five years old when Hitler was elected chancellor in 1933, I still remember the sense of fear that pervaded conversations between my parents and between them and my grandparents. I also vividly recall going out onto our balcony one time when Hitler visited Breslau and seeing him kneeling on the back seat of a limousine, his right arm extended

in the typical Hitler salute. The people on the street went wild with cheers and the inevitable Sieg Heils.

We lived in an apartment, one of perhaps six, on a main thoroughfare. All buildings on this street—in fact, in the entire neighborhood—were destroyed during World War II, and nothing remains today that permits recalling its former status. The apartment we lived in was of the type that we used to call a railroad flat in the United States; it had a very long corridor from which all rooms branched off. My sister and I used to play house under the dining room table using pillows propped up in front of the dining room chairs.

By the time I started school, Jewish children were no longer permitted to attend public school, so I went to a Jewish day school inside the courtyard of one of the major synagogues in Breslau. This courtyard, the synagogue, and the building that housed the school still exist, and I visited it in 1989, in 1998, and again in 2008. Amazingly, despite the Red Army's heavy bombardment of and fighting over Breslau, the windows in the school with the Star of David did not break and look incongruous today in a building that serves mainly as an apartment house.

Two older boys who lived in our apartment house were members of the Hitler Youth, a Nazi-sponsored boys' organization. These boys, together with their school friends, would often try to catch my classmates and me on our way home from school. When they occasionally succeeded, they subjected us to beatings and name-calling. We were quite fearful of these encounters because the police, if they witnessed these episodes, never intervened on our behalf.

By 1937, most Jews had lost their jobs and business owners had been forced to sell their establishment at ridiculous prices to "Aryans." The summer of 1937 saw the sudden and forced displacement of thousands of Jewish men, women, and children who had at one time legally emigrated from Poland into Germany. They were rounded up by Nazi thugs and deposited in the no-man's zone at the Polish-German border. For several days, the Poles

refused to admit these unfortunate people, who suffered from thirst and hunger. Ultimately, international pressure made the Poles admit the refugees into their country, which was almost as deeply anti-Semitic and inhospitable to its Jews as was Germany. One of my best school friends was among these refugees.

KRISTALLNACHT

I am writing this section close to the seventieth anniversary of the day that is often credited as marking the true beginning of the events leading up to the “final solution” of murdering all the Jews of Europe. My family and I were unaware that anything untoward had happened on the evening of November 9, 1938. On the morning of November 10, I got up as usual and left for school, a distance of perhaps a mile and a half. When I exited our apartment building and stepped into the street, I noticed small groups of people congregating in front of several stores. Upon closer inspection, I noticed mounds of broken glass on the sidewalk. As I continued on my way to school, I suddenly saw before me a large crowd, including some of my schoolmates, stopped by a police wooden barricade. Before I even had a chance to talk to anyone, a cry went up from the crowd, “Look, look, the synagogue is on fire.” I could not see the synagogue because it was several blocks away, but I did see a huge column of smoke and fire in the otherwise clear sky. From the location of the fire and the column of smoke, I knew that it wasn’t the nearby Storch Synagogue that was burning. It later became known that it was the Reform Synagogue that had been torched, never to be rebuilt. A small monument today marks the site of the former beautiful, majestic building.

As soon as I heard the news and saw the flames, I turned around and ran home as fast as I could. I told my parents what I had seen and experienced. Within a few minutes of my return, the doorbell rang and two men in civilian clothes entered and identified themselves as Gestapo agents. They told my father that he would have to accompany them and directed him to pack a small bag with socks and under-

garments. Although they could not or would not tell us where my father was being taken, they were polite and not nasty. A short while after they had left with my father, there was a sharp knock on the entrance door, and two relatively young men in black SS uniforms burst into our apartment. They shouted threateningly that they had orders to search our place for weapons. Without even waiting for any reply, they ran into each room and ransacked every closet, drawer, and cabinet, throwing everything on the floor, and knocking furniture over. All this was accompanied by shouts and threats about the “goddamned Jews who were polluting the Reich.” After about half an hour of this activity, they suddenly seemed to have had enough. After uttering a farewell threat, they stomped out, kicking aside the clothes and books and kitchenware they had thrown on the floor.

My mother went to police headquarters to find out what was happening to our father but could get no meaningful answers, except to learn that hundreds of Jewish men had been similarly arrested in Breslau and had been taken to the Buchenwald Concentration Camp. Later we found out that Jewish men had been rounded up throughout Germany and Austria and confined to concentration camps in Buchenwald, Dachau, and Sachsenhausen.

My father never told us what happened to him in Buchenwald, not even years later when we were safely in the United States. I learned some of the details by chance from a Rutgers University graduate who had been picked up outside of Breslau, had been brought to Breslau, and had then joined the men from Breslau on a train to Buchenwald. He described the scene on the train as very crowded, with both police and SS men guarding the prisoners. He pointed out the irony of some of his experiences: A policeman, clearly feeling newly empowered by this job of guarding Jews, went cursing through the compartments and wherever he could would stomp viciously with his boots on an outstretched foot in the aisle, causing great pain and agonized crying. In contrast, the Rutgers graduate also encountered an SS man who surreptitiously slipped a bar of

chocolate to him and another youngster in the midst of all the trauma and chaos. In Buchenwald, the prisoners' heads were shaved and they were forced to stand at attention for hours on end in the bitter cold. They did no useful work the entire time they were there. Some prisoners, mostly older ones who had difficulty standing straight for long periods, were beaten, and some died.

After things had quieted down a bit following Kristallnacht, a friend of my father's inquired with the Gestapo how to get my father released from Buchenwald. Armed with the Iron Cross Medal he had earned in World War I and a visa for entry into Panama, my father was let go on January 6, 1939, with the proviso that he leave Germany within two weeks. It was impossible for the whole family to leave together because only my father had an entry visa for Panama. Thus he left by himself on January 19 on a boat bound for New York because there was no direct connection to Panama within the two-week period that he had to leave Germany. In New York, my father decided that Panama had such a bad climate that he would be better off trying to go to Cuba. It was not yet very difficult to get a visa for Cuba, so my father left New York around the beginning of February 1939 and settled in Havana.

At about the time that my father arrived in Havana, I came down with scarlet fever, which at that time—before antibiotics were available—was a very serious disease. My mother was in the midst of preparing our family to leave Germany to join our father at the end of February. My illness changed all these plans, as I was laid up for nearly two months.

VOYAGE ON THE SS ST. LOUIS

Accompanied by the family friend who had helped get my father out of Buchenwald, my mother, sister, and I left Breslau on May 10, 1939. After a tearful goodbye from our grandparents, we took a train to Hamburg, where the ship was to leave on Saturday, May 13. We checked into a hotel for the nights of May 10 and 11 since we would board the boat on Friday,

May 12. On Thursday, while my sister stayed with our friend, my mother and I went to the Cuban consulate in Hamburg to pick up the entrance permits that had been reserved and paid for the three of us.

The section of the consulate we visited occupied a large room with a counter behind which several clerks attended the public. My mother was rapidly assisted, and, upon presentation of our passports, was given the permits, which cost \$500 per person. As we turned away from the counter and headed for the exit door, a young woman sitting behind a small table to the right of the door addressed my mother: "Madam, would you like me to stamp a visa in your passports? It's free." My mother was taken totally by surprise, and when she regained her composure she replied, "Oh, no, thank you, we just picked up our permits, and I believe that's all we need." How fate often hangs on inadvertent actions that seem trivial at the time of their occurrence! Had my mother agreed to the offer and had the visas stamped in our passports, we might have escaped untold heartache in the months ahead. The passengers of the *St. Louis* who had paid for permits were denied entrance into Cuba 15 days later, whereas a small number of passengers, perhaps 22, who had the visas, were the only ones from among 937 passengers permitted to get off in Havana.

After settling into our stateroom on the *St. Louis*, we went on a short inspection tour. Our first meal, in an elegant dining room, was a major experience: We hadn't seen such quantities and varieties of delicious food in my recollection. We shared a table with a lady and her daughter. Their husband/father, Walter Bardeleben, was also already in Havana. He was Jewish; Anni, his wife, was not, and she was traveling to join him. After the introductions had been made, we discovered that Anni's husband had the same birthday and was the same age as my father. Our families became close friends, and the two men in Havana got to know each other and rented an apartment together. On the *St. Louis* and again later, when we made the transatlantic crossing a second time, Anni

tended to and nursed my mother, who suffered terribly from seasickness.

The St. Louis left Hamburg at 6 PM on Saturday and was pulled by tugboats down the Elbe River to the North Atlantic. Its first destination was the French harbor of Cherbourg, where 38 additional passengers were to board, including my friend from school, Wolfi Feilchenfeld, with his mother and three siblings.

My sister and I had a great time on the St. Louis on the way to Cuba. Although I was only 11 years old, I sensed the freer atmosphere and the absence of the constant surveillance and the chicanery that had afflicted us for so long in Breslau. My sister had Marianne Bardeleben as a friend and playmate, and I found a number of boys on board ship with whom I struck up a friendship.

The voyage from Hamburg to Havana took two weeks. The St. Louis arrived in Havana on Saturday, May 27. The boat was not permitted to drop anchor inside the port of Havana; instead, it did so at Morrow Castle, an island in the bay outside Havana.

ARRIVAL IN HAVANA

None of the passengers had an inkling that we would be denied entrance into Cuba. After we were refused entry, my youth and optimism led me to fully believe that something would happen to permit us to enter Cuba within the next few days. Instead, we were forced to leave Havana unexpectedly a few days after our arrival. The ship cruised off the Florida coast, and at night we could clearly see the lights of Miami. I have read (although I did not know this at the time) that several groups of young men, with the help of some sailors, were prepared to man lifeboats and row to shore. This plan was scuttled when two Coast Guard cutters appeared and told the captain of the St. Louis to immediately leave the area and move into international waters. Many telegrams were sent to President Roosevelt, asking for his intervention, but to no avail.

A committee of passengers on board the St. Louis worked closely with Captain Schroeder,

the very decent captain, to try to arrive at a solution to our dilemma. The captain was determined to not take the ship back to Germany, where our fate would have seriously hung in the balance. The captain, it was later discovered, had made plans—which he did not even share with his committee—to take the St. Louis off the coast of Scotland and to scuttle and burn the boat to force the British authorities to take us in. Very fortunately, this did not become necessary. A knowledgeable and well-connected representative of the Joint Distribution Committee (hereafter referred to as the Joint), an American charitable organization that is to this day financially and politically assisting Jews worldwide, was able to convince the governments of England, France, Holland, and Belgium to each take in about one-fourth of the refugees. Thus it was that on Saturday, June 17, 1939, the St. Louis landed in Antwerp, Belgium, and 900 passengers were divided up, mostly by lot, and assigned to one of the four countries listed above. The passengers for Belgium stayed in that country upon disembarking and most took a train to Brussels. My friend Feilchenfeld and his family were among this group. The passengers for Holland took a train to that country, and those going to England and France were transshipped via another two boats that were already waiting in Antwerp. My mother, sister, and I were assigned to go to France, a voyage that took no more than a day. The ship from Antwerp landed in Bourgogne, France. From there, my mother, sister, Anni Bardeleben, and her daughter took a train to Laval in the province of Mayenne. I, however, together with all children over age 10, was sent to a children's camp, in Montmorency, a suburb of Paris.

France

I stayed in Montmorency from June to the beginning of November 1939.

On September 1, 1939, Germany invaded Poland in a blitzkrieg, and France and England declared war on Germany. Shortly thereafter, amid the great, early successes of the German

army, there were air raid alarms around Paris, with German planes flying overhead and occasionally bombing certain sites. At Montmorency, we spent much time in an air raid shelter in the basement of our building. By the middle of October, we spent most nights in the air raid shelter and got very little sleep. When we reentered our normal living areas in the morning, the stairs leading to the shelter were a sight to behold: Every step was littered with our favorite belongings—dolls, stuffed animals, books, and the like. Finally, at the end of October, my mother was able to arrange to have someone pick me up and bring me by train to Laval to join her.

Laval

When I arrived and descended onto the cobblestoned streets of Laval, I felt as though I had been transported back in time to the middle ages. Located in the center of France, Laval had a population of 39,000, in the 1960s. To the best of my knowledge, in 1939 there were no homes with running water, no indoor toilets, and the lifestyle was primitive. Food, however, was very plentiful.

One day, a very fancy carriage pulled up in front of our inn, and a liveryman got off and asked for my mother, Madame Fisher. When my mother approached, he announced that his master, a wealthy owner of an estate nearby, wanted to invite us to his home. My mother made the necessary arrangements, and several days later the same carriage appeared to take us to the estate. It was a beautiful place, in the midst of apple orchards and other trees that were just changing color in the nippy fall weather. When we stopped, I couldn't resist picking up a small, completely red apple that looked terribly inviting. And so I bit into it, only to spit it out as quickly as I could for it was gall bitter. The liveryman laughed and told my mother that these were French cider apples that were not sweet like normal eating apples.

The owner of the estate came out to greet us, very formally dressed. He was an older

man, perhaps in his late sixties or early seventies. He invited us into a well-decorated living room, and we were served tea and some cake. Our host then proceeded to tell us the reason for his invitation. He said that the village priest had preached for decades that Jews had horns on their heads, and because our host had never before met a Jew, he wanted to see for himself whether this was true. He admitted to having been skeptical, but he really didn't know. This occurred in November of 1939 in France!

One day, newcomers arrived in Laval and at our inn: British soldiers. The war was ongoing, and Britain was beginning to ship soldiers across the channel. I remember how some of these fellows got stone drunk on French wine because they were used to drinking beer, not wine. Our monotonous routine was eventually interrupted by a telegram informing us that my father and Mr. Bardeleben had obtained visas, once again, for the five of us (the three Fishers and the two Bardelebens) to travel to Cuba to join our fathers.

We left Laval by train, bound for Le Havre, where we would board the liner *DeGrasse*, which was once a well-known luxury ship but had been long out of service before it was recalled for war-time tasks.

We arrived in Le Havre in late afternoon and had hardly gotten off the train when we were caught in an air raid. As we walked toward the station's exit, we suddenly heard a tremendous explosion. A bomb had hit the steam locomotive of our recently arrived train, and we felt the explosion pull and drag us along the cement platform on which we had been walking. We all had numerous bruises, and we thanked our lucky stars that the car we had been in was at the very rear of a long train and thus was far removed from the engine that had been hit by a German bomb. After the commotion died down a bit, we were able to make our way from the train station to a hotel across the street, where we stayed overnight. At least two more air raids occurred that night, but we ignored them and did not go down into the hotel's basement shelters.

The next morning we boarded the DeGrasse. Our cabins were far down on one of the lower decks, below the waterline. I have no recollection of leaving Le Havre, but we probably departed at night so as to escape German attempts to bomb ships leaving harbor. Our first part of this voyage was of very short duration—we only crossed the English Channel to Southampton, which was a major British port then as it is today. We remained at anchor in Southampton for nearly two weeks, until a convoy of approximately 200 ships had assembled that was bound for New York, and we were escorted by British cruisers and warships. Between the outbreak of World War II in September of 1939 and the end of that year, German submarines had sunk 114 merchant ships, mostly British. It was the end of December when we finally left Southampton, and the weather in the North Atlantic was miserable and stormy. My poor mother, who had suffered from seasickness on the St. Louis when the weather had been near perfect, was now seriously ill as the DeGrasse tossed and turned in the Atlantic. Anni Bardeleben deserves sole credit for getting my mother to New York alive. I did not suffer at all from seasickness and was one of very few passengers in the dining hall during our five-day crossing.

And then, there she was: the Statue of Liberty! Tears streamed down many of our faces as the DeGrasse pulled past her. We docked, I know not where, but our little group was not allowed to leave. After immigration officials had inspected our papers, we were transferred to a small boat that took us to Ellis Island, where we awaited the next boat from New York to Havana.

The passage from New York to Cuba on a luxury cruise liner was pure pleasure. The food, the good weather, and my mother's improved health once we left the cold north all contributed to a very good feeling that the tide had turned. Many of the passengers who had learned of our earlier odyssey pampered my sister, Marianne Bardeleben, and me. Before we knew it, we had docked in Havana and were

reunited at long last with my father, and the Bardelebens with their dad and husband.

A YEAR IN HAVANA

The year 1940–1941 was a difficult one for those of us who had close relatives still left behind in Germany. I am sure that we received some mail from my grandparents Gottheiner informing us that they had been moved by the Nazis, first to a small town, Tormersdorf, and from there to Theresienstadt Concentration Camp where they, as well as my grandmother Fisher and my aunt Hilda, were to die of starvation and disease. Although their death was made known to us only after the war, my mother became deeply depressed even at this stage following the first deportation, and she attempted suicide sometime in 1940. Fortunately, we had Dr. Bardeleben, a physician, living with us, and he was most helpful to get her to vomit the pills she had swallowed.

Another problem we faced in Havana that clearly affected my mother was our poor financial situation. I believe we received a small hand-out from the Joint. Officially, my father was not allowed to work, but before we arrived he had started a small peddling business selling shoemaker supplies, rubber heels, shoelaces, leather for soles, and the like. He carried two very heavy suitcases and went from one shoemaker in downtown Havana to the next. I accompanied him after school, also carrying two suitcases that were very heavy, and in the broiling Cuban weather we were always soaked in sweat. Many shoemakers could not pay the full price and my father, if he wanted to make a sale, had to give credit. I learned important lessons during this period from the shoemakers, who were friendly people and often told us their life's story. A large number were Armenians whose parents had left during the persecutions in Turkey during World War I. Some of the horrific experiences they related in their stories equaled the atrocities we would later learn that the Nazis perpetrated against the Jews.

I vividly recall my happiness when we left Havana for New York City in February 1941. I had often felt hemmed in and almost claustrophobic in Havana, primarily because I couldn't tolerate the extreme heat, which differed between summer and winter only in relation to the level of humidity. It was either hot and humid or hot and less humid. The thought of being forever subjected to that climate was difficult for me to accept at age 12.

NEW YORK CITY

After we arrived in New York City, we stayed in the apartment that the Bardelebens had rented for us only a short time, perhaps a week, after which we moved to an apartment on 93rd Street between West End Avenue and Riverside Drive. My mother immediately found work as a baby nurse. This paid fairly well and essentially sustained our family. My father, who was 50 years old, had a very hard time and could not find a job. The United States had not yet entered the war and was still suffering from the effects of the Great Depression. My father tried to find something in the shoe industry and traveled to New England, where there were several large shoe manufacturers, but to no avail. In the summer of 1941 my parents made the decision to try their luck at poultry farming. The Jewish Agricultural Society made mortgages available at very low cost and helped provide the training to start a farm.

Meanwhile I went to public school, and although I didn't know any English, I picked it up very rapidly in the environment where everyone spoke that language. After school I tried to earn a little money and tried my luck, together with other boys, in front of the nearest A & P market, carrying packages for women who had done their shopping. One would typically get 10–25 cents depending on the size of the package(s). Since the competition was fierce and the conditions, including weather, were not always satisfactory, I decided to look for a more stable, permanent job. With a bit of good luck, I found a job in a cleaner/laundry store where I also did the deliveries for customers. I earned \$2

a week working after school and also received tips. I saved the salary religiously and after three months was able to buy my first brand-new bicycle for \$24!

I attended public school in seventh grade from the time we arrived in February until the end of that school year in June. It was difficult at first because I didn't know any English, but I made friends with a couple of boys from the neighborhood, and they helped me with homework.

Later in the summer of 1941, my parents took a course in Bound Brook, New Jersey, to prepare them for their upcoming farming experience. In September they bought a small, rather run-down farm, and we moved to Vineland, New Jersey.

The Vineland institution that was to have a profound influence on my life was the Free Public Library. Without a doubt, this kid, who was in the country less than a year and still did not speak fluent English, became one of the library's best clients. A kindly librarian took me under her wing and introduced me to a wealth of literature, mostly British, that enchanted me and made an otherwise difficult adjustment much easier. Among the authors whose works I devoured was Warwick Deeping, whose *Sorrel and Son* was simply enchanting. P.G. Wodehouse and Jeeves were hilarious and most entertaining, as were Alexandre Dumas' adventure stories, *The Three Musketeers*, *The Count of Monte Cristo*, and biography of the notorious Lucrezia Borgia and her family. Walter Scott's *Ivanhoe* and Rafael Sabatini's *Scaramouche* and *Captain Blood* also were books I found exciting as a 14- and 15-year-old.

THE FARM

As exciting as the transition from city to farm life may have appeared, the adjustment was far from easy. The farm buildings were all in poor condition and required a great deal of repair. To bring in carpenters, plumbers, and electricians was far beyond my parents' financial capability. And neither of them had the know-how or dexterity to carry out such repairs. I suffered

greatly when I saw my parents despondent over the continuous major and minor problems that made their progress at successfully managing the farm so very difficult. In the spring of 1942, I obtained an after-school and weekend job on a nearby farm owned by a wealthy family. My job was to help a caretaker with his chores, mainly repairs. Through this man, I soon picked up considerable skills in carpentry, plumbing, and roofing, which allowed me to begin the seemingly endless task of repairing our own farm buildings. My meager salary was spent purchasing the tools and supplies without which repairs were almost impossible to carry out. Over time, I replaced all the water lines on the entire farm and fixed all the roofs, among many other chores.

Another serious problem we encountered on the farm was that it was overrun by rats. If one ventured into a chicken house at night, one would literally trip over these rodents, some of which were the size of kittens. We were fortunate to acquire a dog that turned out to be a terrier with an innate instinct to hunt and kill rats. Every night after dark the dog would come to nudge me, and precede me at a run to the different buildings. Within a few months, the rodent problem had been reduced to more manageable levels. However, only when a chicken house was completely empty was I able to really clean up by fumigating with a vacuum cleaner hose inserted into the exhaust of a car on one end and the other end placed into a rat hole that was not too difficult to find. I am sure there were initially more rats on our property than there were chickens.

Although the farm's produce—eggs, chickens, and milk, butter, and cottage cheese from two cows—permitted us to have an adequate food supply, the farm never provided a decent profit. During the time that we owned the farm, my father was in continual debt to the feed dealer. I sold the farm after my father passed away in 1969, and more than half the proceeds were paid back to the dealer who had long given up on this money, for which he never charged interest!

HIGH SCHOOL

We arrived in Vineland in the fall of 1941, sometime after school had already started. I was placed in eighth grade but have no recollection of that last year before high school. The following year I started high school. I met several nice boys who became friends, and in general I enjoyed the curriculum and my classes and teachers.

One of the most important subjects I had in high school was Latin. I took the first two years in Vineland High School and then had private lessons with a paraplegic lady who was a retired teacher and knew her Latin very well. I am convinced that my study of Latin was instrumental in my learning English grammar, spelling, and vocabulary, and was the reason I excelled in writing when I entered college.

In the fall of 1945, a friend joined forces with me to start a business repairing roofs on farms; eventually this led to a vaccination service. Chickens were vaccinated against three major diseases that afflicted them and could wipe out an entire flock: chicken pox, laryngotracheitis, and Newcastle disease. The latter two vaccines had been developed by Dr. Fred Beaudette, a veterinarian at Rutgers University. When I started to attend Rutgers in the fall of 1946, I took a class with Beaudette and used my acquaintance with him to advertise our vaccination business. The income from our business saw both my partner and me through our undergraduate studies at Rutgers.

THE UNDERGRADUATE YEARS AT RUTGERS

My curriculum was very heavily oriented toward biological sciences. I took courses in genetics, microbiology, biochemistry, and zoology, and I completed enough chemistry courses to graduate with a minor in that subject. I generally earned good grades except for one semester, when I slipped up in physics and in calculus because I was preoccupied with my social life and didn't study for a top grade. Two professors made a greater-than-average impression on me: Professor Platt, who taught nutrition and

had an inquisitive mind that rubbed off on me, and Professor Roth, who taught biochemistry. The latter basically directed my future course of study and contributed to my ending up as professor of nutritional biochemistry.

One month after graduating from Rutgers, I traveled to Chile. There I met the daughter of family friends, and we got married at the end of July 1950. I entered the University of Connecticut as a graduate student upon my return to the United States.

AN M.S. FROM THE UNIVERSITY OF CONNECTICUT

My advisor was Lloyd Matterson, a good analytical chemist from whom I learned much in the way of laboratory technique. The department chair was Dr. Edwin Singesen, who was a bit taciturn but had a good relationship with the agricultural community. Two other graduate students with assistantships similar to mine started in the department that fall. Our duties in return for the assistantship consisted primarily of mixing feed for the large poultry flocks maintained by the department. Legally we were obligated to work 15 hours per week, but this time period was often adhered to only in the breach.

One day in the winter of 1951, such extreme stress was placed upon the three of us in terms of the time required to mix enormous amounts of feed (in an unheated, dusty barn) that we told our supervisor, who worked for Singesen, that we would not continue beyond our required 15-hour limit. She promptly complained to Dr. Singesen, who shouted at us and threatened us with dismissal. I became the ringleader in convincing my colleagues to call Singesen's bluff. They agreed to go along. We handed Singesen a letter of resignation and went to see the Dean of the Graduate School who greeted us most cordially. He listened to our story and then surprised us no end by telling us that we were not the first ones to have been so abused, that this had happened before, and that he would be happy to write a strong letter of recommendation for each of us to other universities to which

we might wish to transfer! We were elated and optimistic about our future. We had all been enrolled in the doctoral program at Connecticut, but with this turn of events we each decided to accept a Master's degree and to move on.

Two professors at Connecticut left strong impressions on me: Hamilton Eaton, a dairy nutritionist, and Geoffrey Beall, a biostatistician and colleague of R. A. Fischer, who had catapulted biostatistics into a powerful tool in the life sciences. Eaton imbued in me the importance of keeping up with the scientific literature. He regularly reviewed Chemical Abstracts, an abstracting service that covered most scientific journals published, regardless of language. Beginning in 1951, I too started to review Chemical Abstracts and did so until 2005 when I stopped my subscription. Eaton also imbued me with the importance of using mathematical statistics in designing and ultimately evaluating the results of experiments. He introduced me to Beall, a very smart and astute biostatistician. I still have my notebooks from his two courses, which have been invaluable in applying statistical methodologies to my experimental work over the years.

As I mentioned above, in the winter of 1951–1952 my fellow graduate assistants and I had a fall out with Dr. Singesen, the chair of the department. Dr. Whetten, the dean of the graduate school, advised us to apply to the University of Illinois because Dr. Scott had moved to this institution after leaving the University of Connecticut, following his own fall out with Singesen.

All three of us received acceptance letters from Dr. Scott at the University of Illinois. One of the three of us was also accepted at Cornell and went there. The third fellow student decided to go to Iowa State because a personal problem had come up while Dr. Scott was away from campus and he needed to resolve the matter quickly.

Although I originally had been in the PhD program at Connecticut, I had earned enough credits and even research accomplishments for an M.S. degree, which I received at graduation ceremonies in May of 1952 (the only time I

attended a graduation for one of my three degress). After graduation, my wife, Ruth, and I packed our few belongings into the car. On June 3, we left the east coast and drove to Urbana, Illinois.

THE UNIVERSITY OF ILLINOIS

June 5, 1952, the day I arrived in Urbana, was an exceedingly hot day, with temperatures over 100°F. Dr. Scott had the two of us from Connecticut stay at his house until we could find accommodations. When I arrived at the Scott home, Mrs. Scott greeted me warmly and told me that her husband was attending the graduation ceremonies at the university stadium. Soon thereafter Dr. Scott arrived, sweating profusely, his shirt completely soaked. He informed us that only seven people had passed out from the heat and had been taken to the hospital. He showed me the graduation program, which I found most impressive: 90 students had received their PhD in organic chemistry! Compared with Connecticut or Rutgers, the University of Illinois was enormous, indeed! Upon touring the campus, which straddled two adjacent towns, Urbana and Champaign, it became clear just how large the university was. The chemistry building alone could have housed all the departments from the College of Agriculture at Rutgers.

The two years we spent in Illinois were among the most enjoyable imaginable. The university had so much to offer us, not only me but for my wife, Ruth, as well. Ruth, a talented musician who played violin and recorders, was able to join the university orchestra and had the pleasure and honor to play under Ernest Ansermet. She met a member of the music faculty, George Hunter, who opened a new vista of music for Ruth on the recorder and other old instruments. She also became familiar with the madrigal literature and to this day sings with a quartet on a regular basis. Last, and most importantly, she was asked to join a faculty string quartet and thus became exposed to the vast and beautiful chamber music literature. Ruth played with the wife of the chairman of the Microbiology

Department, Dr. Gunsalus (Gunny), and with a famous entomologist, Dr. Fraenkel, the discoverer of the role of carnitine in metabolism.

For me the University of Illinois was an absolute eye opener. The university excelled in all the major sciences that are pertinent to my field of study, nutritional biochemistry. All the courses that I took in biochemistry, nutrition, physiology, statistics, and others were cutting edge, and the faculty members were among the best not just in the United States but also in the world. In biochemistry, William Rose and Herbert Carter were the stars, among many other good professors. In 1935, Rose had isolated and discovered threonine, the last of the essential amino acids. Using his graduate students as guinea pigs, Rose went on to determine the amino acid requirements of human beings, a task that took some 10 years to complete.

Herb Carter was an outstanding organic chemist who turned his attention to biological substances and determined the chemical structure of some early antibiotics. Both he and Rose were also exemplary teachers, and I recall to this day their superb and inspiring lectures.

In the Nutrition Division, H. H. Mitchell stood out as a giant among many other very talented colleagues. Mitchell's course in Comparative Nutrition set me on my future career path as no other single course ever did. Every aspect of nutritional science was equally well covered in this course with a depth and thoughtfulness that is indeed rare in any discipline. I felt challenged throughout my stay in Illinois, as I continued to be in my later career, to explore the literature well beyond the needs of passing the courses and even of getting decent grades. Mitchell stressed the importance of mathematics in the biological sciences. If one couldn't describe a life process, such as growth, in mathematical terms with an equation that had predictability value, it wasn't science. He would give very complex problems for homework assignments that took hours, sometimes days, for us to research and that we would discuss and argue about late into many a night.

Although Dr. Scott initially provided my assistantship while at the university, my

immediate advisor was B. Connor Johnson, a bright, lively Canadian who challenged me in other ways in my laboratory research. Thus, I learned the use of radioisotopes, C^{14} , in studying the vitamin niacin and its excretory products in chickens.

Since birds void urine and feces together and not separately, as is the case in mammals, I developed a surgical procedure to obtain pure urine in order to study the niacin metabolites.

Another accomplished biochemist in a different department, Gaurth Hansen, was engaged in the study of galactose metabolism. Galactose is the sugar that, together with glucose, is utilized by mammals to synthesize lactose, or milk sugar. Interestingly, galactose is very toxic and poorly tolerated by chickens, and Hansen wanted to better understand its metabolism in this species. He approached me to help provide him with operated birds so that he might obtain pure urine for his studies. This led to a highly productive collaboration that resulted in a landmark publication in the journal *Analytical Chemistry* (11). The problem that I attempted to solve was to determine simultaneously the glucose and galactose content of urine and blood. This became possible by reading solutions at two wavelengths in a photometer and solving simultaneous equations. We ordered 400 reprints of the article, and they were gone in less than two weeks. My PhD thesis was on tryptophan and niacin metabolism and resulted in several publications in the *British Journal of Nutrition* and in the *Archives of Biochemistry* (14, 15).

I graduated in June 1954 with straight A's in all courses and nine refereed publications. Several weeks after graduation, I was hired by Rutgers University as Assistant Professor of Nutritional Biochemistry in the College of Agriculture.

One of the people I met at Illinois was a fellow graduate student, Paul Griminger. We became good friends, and three years later, when I had an offer from Johns Hopkins (while at Rutgers), my dean offered me the opportunity to bring a colleague to join my nutrition program. I immediately thought of Paul, who, in

the meantime, had moved to the University of Nebraska. He came for an interview and was hired by the dean, leading to a long scientific collaboration and personal friendship.

RESEARCH ACCOMPLISHMENTS AND MY YEARS AT RUTGERS

I have spent more than 52 years at Rutgers University, rising through the ranks and serving as the first chair of the Nutrition Department, beginning in 1966 and continuing for 22 years, followed by several years as Associate Provost for the Life Sciences. I also chaired, for many years, the Committee on Standards and Priorities in Academic Development, whose task it was to periodically review and evaluate, with the help of experts from major universities, all Rutgers departments, programs, and institutes. The variety of duties and experiences during all these years was interesting and exciting, but nothing could compete with the enjoyment and satisfaction I derived from my research, my contacts with bright undergraduate and graduate students, and the teaching of several courses on a regular basis.

I was very fortunate to have been the recipient of federal, industrial, and foundation grant support throughout my career. I supervised 42 M.S. and PhD students, most of them the latter. I also had the good fortune to supervise eight very bright postdoctoral fellows and to collaborate with many excellent colleagues from Rutgers and other universities, including a pathologist from the University of Edinburgh. An outstanding scientist from Niigata University in Japan also spent one and a half years in my lab.

Amino Acid Requirements

My research career has touched on a number of interesting topics that have led to some noteworthy discoveries. My PhD thesis research concerned the essential amino acid tryptophan, and amino acids remained an important area of my investigative interests. Immediately upon arrival at Rutgers, I carried out a series of

experiments designed to formulate an amino acid-containing diet for hens that would maintain egg production and then to follow up and determine the essential amino acid requirements for egg production. After much trial and error, these studies were successful (12, 23, 24) and led to further experiments designed to determine the maintenance requirement of adult male chickens. Gil Leveille carried out these studies for his doctoral thesis.

In the course of these studies, we made the interesting observation that although the amino acid histidine apparently was not required for nitrogen balance over the short term (2–3 weeks), it nevertheless was needed over the long run. Without dietary histidine there was a sharp drop in the histidine-containing muscle component, carnosine, a dipeptide. This finding, which we recorded in a publication in 1960 (28), would become the focus of a fascinating and challenging research project nearly 20 years later.

We also determined the amino acid requirements of rabbits (1) and reassessed the requirements of adult women (6).

Cholesterol and Avian Atherosclerosis

At about the time that the above-mentioned and other amino acid studies were ongoing in my lab, I received a visitor, E. H. (Pete) Ahrens, Jr., from the Rockefeller Institute (now Rockefeller University) in New York City. Dr. Ahrens wanted to know what I thought of the idea of altering the lipid composition of egg yolks. Could it be done? I told him that I had no idea, but I would investigate and let him know. A literature review came up with only two articles on the subject, with both suggesting that it might be feasible to change the composition of the fatty acids in egg yolk and turn them more unsaturated. Dr. Ahrens had recently published an important article (2) showing that unsaturated fats, such as corn oil, could reduce blood cholesterol in people with high cholesterol levels, in comparison with the ingestion of saturated fats such as butter. Because egg yolk also contained appreciable amounts of cholesterol (about

250 mg for a large-size egg) and had a high saturated fatty acid content, Ahrens wanted to explore the possibility that consumption of eggs with a higher unsaturated fatty acid content might lead to lower blood cholesterol levels.

We undertook some preliminary experiments, feeding hens differently saturated fats and checking the composition of the eggs produced by these hens. The hens did, indeed, incorporate more unsaturated fatty acids into the egg yolk when the diet provided such fatty acids (13). A byproduct of these studies was the beginning of a major investigation in our lab of atherosclerosis in the chicken.

Upon presenting our results to Dr. Ahrens, we decided to go ahead and produce two types of altered eggs: one from hens fed a high linoleic acid-containing diet and the other from hens fed a high linolenic acid-containing diet. The eggs were produced in sufficiently large numbers so that Ahrens could feed them to patients at the Rockefeller Hospital who suffered from hypercholesterolemia. The results were unexpected: Instead of lowering the blood cholesterol levels of patients with high blood cholesterol, the altered, more unsaturated eggs elevated blood cholesterol. In time, it was discovered that the high-unsaturated fatty acids enhanced absorption of the egg cholesterol. Thus, dietary cholesterol is poorly absorbed in the presence of saturated fat, but is better absorbed when consumed together with a rich source of unsaturated fat.

While these studies were ongoing, we obtained serious funding from the National Institutes of Health (NIH) for our cholesterol and atherosclerosis work. We were fortunate to enlist the collaboration of two special colleagues: Harold Weiss, a physiologist who was interested in blood pressure problems and also used the chicken as his animal model, and Walter Siller, a veterinarian at the University of Edinburgh who specialized in the histology of avian diseases, including atherosclerosis.

Among our findings in this field of study were the following: Hens, during their egg-producing phase, do not get atherosclerosis as exemplified by fatty deposits in the aorta. This

is similar to observations in premenopausal women who are unlikely to get heart disease, presumably due to protection from the hormones estrogen and progesterone. On the other hand, adult cockerels invariably showed considerable plaque formation in the aorta and coronary arteries, often leading to severe occlusion, which Dr. Weiss was able to quantify and Dr. Siller was able to confirm histologically (7). We also observed that plant sterols were effective in lowering induced high blood cholesterol levels (26).

In about 1960, the U.S. Army Quartermaster Corps asked us to evaluate the atherogenic properties of Army C rations that had been used during the Korean War. Autopsies of young soldiers killed during that conflict showed a high incidence of the beginnings of atherosclerotic plaques, and the Army was concerned that the diet might have contributed to this condition. C rations that had been frozen since the war were shipped to us, and we mixed together 12 different menus to feed to chickens for a period of 18 months. We ran into a major problem: The mix was so viscous that the birds could not eat it properly; it would stick to their beaks and prevent proper food ingestion. Furthermore, the high moisture content of the mixed diets, about 50%, made them very susceptible to bacterial and mold growth. We resolved these technical problems by adding calcium silicate, a material that absorbed seven times its weight of liquid, and we found that dried sugar beet pulp worked just fine to improve the flow characteristics of the diet. At the end of the 18-month trial, to our astonishment the birds on the Army ration had a lower incidence of atherosclerotic plaques than the controls (16)! Ancel Keys, a well-known epidemiologist of heart disease, had reported (25) that Italians consuming a diet high in grapes and apples had a lower incidence of heart disease than did Italians who did not consume much in the way of these and other fruits. He suggested that pectin in the fruit might be responsible for this observation. I checked on the pectin content of various fruit compotes that were part of the C rations. None of the fruits were particularly high in pectin. As I was about

to close the book on pectin, my attention was drawn to a footnote on the page opposite the one I had been reading. There it was, "until the late thirties pectin was produced commercially in the US from *sugar beet pulp*." It turned out that sugar beet pulp contained about 33% pectin. We had included it at 10% of our diet, thus supplying more than 3% pectin. I rushed back to my office, called the Sunkist Corporation, and ordered 50 pounds of pure pectin. Two months later, following a short preliminary experiment, we had our answer: Pectin lowers blood cholesterol, and it seems to do so by binding to cholesterol, leading to its excretion in the feces and thereby retarding the onset of atherosclerosis (9). After many other studies with pectin in rabbits, pigs, and humans, we also tested other fiber sources for their cholesterol-lowering efficacy and discovered that oats and barley had good potential in this regard (8). In 1985, together with writer Eugene Boe, I published *The Rutgers Guide to Lowering Your Cholesterol: A Common Sense Approach*. The paperback edition, published by Warner Books, Inc., sold 100,000 copies.

Carnosine, Histamine, and Wound Healing

In 1975, a graduate of our program who had obtained her PhD with Paul Griminger joined the Monell Chemical Senses Center at the University of Pennsylvania as a postdoctoral fellow. Eunyong Chung called me shortly after arriving at the University of Pennsylvania and asked my advice concerning an interesting research project she might work on, which would span both the fields of nutrition and of the chemical senses, taste or smell. After thinking about it, I told her that I had just read an article in *Science* (30) that reported finding large amounts of carnosine present in the olfactory bulb of rats, with the suggestion that carnosine might be the chemical transmitter for smell. I then told Dr. Chung that we had observed 20 years earlier that in chickens on a histidine-free diet, carnosine concentrations in muscle were significantly reduced. I suggested that she try to check out

the hypothesis that feeding a low-histidine diet to rats would lead to reduced carnosine in the olfactory bulb. If carnosine indeed was the neurotransmitter for smell, such a diet treatment should interfere with the rat's ability to detect odors.

Eunyong thought well of the idea, as did the faculty at Monell. Although the feeding of a low-histidine diet was very straightforward, the analysis for carnosine was not. It took Eunyong close to a year to develop a gas-chromatographic method that was accurate and repeatable. When she finally ran her first feeding trials, she was able to show unequivocally that a low-histidine diet reduced the concentration of carnosine in the rat olfactory bulb (4). By this time, she had found a good position in Washington, D.C., and she left Monell.

Even before Eunyong left, I was engaged by the director of Monell, Morley Kare, to serve as a consultant to the Institute. With my input, Michael Quinn was accepted into a joint PhD program between Rutgers and Monell. I became his major advisor, and he took his courses at Rutgers but carried out his lab work at Monell. I applied for NIH funding for the carnosine project, with both Rutgers and Monell sharing the funds. The proposal was funded. We learned a great deal about histidine and carnosine, but the original hypothesis that carnosine played a role in the olfactory pathway turned out to be incorrect. Having invested so much time and effort on this project, I was determined to find a real function for carnosine. My graduate students and I spent much time going through the scientific literature seeking a meaningful clue. It was not long in coming.

During his studies of olfaction and carnosine, Michael Quinn had noticed that rats that were on low-histidine diets and that had reduced carnosine concentrations in muscle and olfactory bulb were unusually nervous (34). We surmised that these animals were stressed and found evidence in the scientific literature suggesting that histamine plays an important role in stress metabolism. My older son, David, who was 20 years old at the time and attending Swarthmore College, spent the summer of 1977

at Rutgers in the lab of a colleague in the Biochemistry Department. David came up with the suggestion of producing an acute injury in rats and chicks and measuring the consequences on carnosine levels in the afflicted versus nonafflicted tissues. The results were dramatic. We made mild incisions in the muscle of one leg of a chicken (under anesthesia) and 24 and 48 hours later measured the carnosine content of the muscle tissue in both legs. The muscle with the incision showed a 27% decrease in carnosine content compared with the uninjured muscle tissue. We repeated this type of experiment in rats where we fractured (also under anesthesia) one femur bone and left the other side intact. We also injected either histidine or histamine into some animals. The carnosine decrease in the tissue adjacent to the fractured leg was just as dramatic as it had been in the incised chicken muscle. The injections with histidine and histamine *completely prevented* the reduction in carnosine (5).

With these findings, we expanded our experimentation. We showed that animals inoculated with pathogenic bacteria also showed sharp decreases in their body carnosine concentration (17). Dennis Fitzpatrick, a new graduate student from Canada, carried out sophisticated experiments of measuring the tensile strength of sutures in rats that had been injured by incision, followed by injections with carnosine itself or with histidine. We observed very significant improvements in tensile strength that amounted to faster healing in the injected animals (18).

At the time that these studies were ongoing in our lab, a young surgeon, Louis Flancabaum, who had just taken up a position as a trauma surgeon at Robert Wood Johnson Medical School in New Brunswick, came to visit and to ask if he might work and learn in my lab. The carnosine studies were of great interest to him in relation to his specialty, trauma treatment. He, together with two residents training under him, collaborated with us for close to 10 years on a variety of studies, all related to histamine and carnosine metabolism (3, 19). I also had the good fortune to have the assistance on this project of Dr. Teru Ishibashi, a professor from Niigata University

in Japan, who spent a year and a half in my lab. He studied the interrelationship between dietary histidine and carnosine concentrations in various tissues in the chicken and the rat (21, 22).

I have always felt that there was still more to the carnosine story, particularly as it applied to the olfactory bulb. The olfactory nerve is the only nerve that spontaneously regenerates in mammals. Histamine is known to play an important role in growth and reproduction. Might the high carnosine level in the olfactory bulb bear a relationship to this nerve regeneration? A few years ago, researchers in England showed (29) that implanting ensheathing cells from the olfactory bulb into rats with severed spinal nerves was effective in bringing about regeneration. Ensheathing cells are the ones that produce the carnosine that is stored in the olfactory bulb. This is a problem still awaiting resolution.

Studies on Ethanol

A by-product of the histidine-histamine studies was the observation that a high intake of pyridoxine and of histidine stimulated the activity of the enzyme histidine decarboxylase and increased histamine production (27). We then found that, analogously, on a high-pyridoxine and an elevated tryptophan intake, the activity of 5-hydroxytryptophan decarboxylase and the serotonin level in rat brain were significantly elevated (27). In collaboration with Dr. Wagner, a neuropsychologist from the Rutgers Psychology Department, we carried out a multifaceted series of studies that involved alcohol metabolism, much of it related to serotonin and its precursor amino acid, tryptophan.

Three major accomplishments resulted from these experiments:

1. We found that during alcohol dependency, serotonin in the brain decreased and dopamine, another neurotransmitter, increased (31). Dr. Mirovsky, a post-doc from Israel, had the brilliant idea, not previously recognized, to combine

two drugs simultaneously in treating alcohol craving and its withdrawal symptoms. There had been limited success with individual drugs that affected either serotonin or dopamine, but no one had tried a combination. Mirovsky was successful in treating the chronic toxicity of alcohol with two drugs that became very popular for weight loss at about the time she discovered their potency vis-à-vis alcohol: phentermine plus fenfluramine (32). These drugs were used by millions of obese patients as an effective weight loss medication until the U.S. Food and Drug Administration withdrew fenfluramine from sale because of several deaths due to heart valve problems. These same drugs were also very potent in the treatment of chronic alcoholism.

2. We noticed that the diet consumed in conjunction with alcohol greatly influenced alcohol's toxicity. On a high-carbohydrate, low-fat diet, alcohol was metabolized rapidly, resulting in low blood alcohol levels and reduced incidence of withdrawal seizures compared with a high-fat, low-carbohydrate diet (10).

Recently, we have also studied the alcohol-induced fatty liver condition that accompanies chronic alcoholism. The high-carbohydrate, alcohol-containing diet sharply reduced liver fat compared with a high-fat, alcohol-containing diet. It has long been believed that the fatty liver condition produced by alcohol consumption is related to oxidative damage. Thus, antioxidants such as vitamin E were believed to be protective. We have shown, however, that vitamin E and selenium, another compound with antioxidant properties, can be pro-oxidative at high intakes. A synthetic antioxidant, DPPD, was found to be very effective as an antioxidant without pro-oxidant qualities and, together with caffeine, to lower liver fat significantly in the alcohol-consuming rat (33).

3. Finally, we have shown that a derivative of our old friend tryptophan, 5-hydroxy-L-tryptophan, in combination with phen-termine is as effective as fenfluramine in reducing withdrawal seizures and alcohol craving and thus is a potential substitute for the fenfluramine, a drug no longer permitted to be used (20).

CONCLUDING REMARKS

I have enjoyed a career in research and teaching in an academic setting that was challenging and exciting. My success in advancing several areas of science has been coupled with the

good fortune to have had a most supportive wife for more than 57 years and three children who have all advanced successful careers. Our daughter, a clinical psychologist, is Deputy Director of an organization that operates 22 homes for physically and mentally retarded adults; one son, an oncologist, is Chief of Dermatology and Director of the Melanoma Unit at Massachusetts General Hospital in Boston; and our younger son is Director of Interventional Cardiology at University of Massachusetts Medical Center in Worcester. And last, but certainly not least, we have 10 precious grandchildren—7 boys and 3 girls.

DISCLOSURE STATEMENT

The author is not aware of any biases that might be perceived as affecting the objectivity of this review.

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Errata

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