

Edwin G. Krebs – Autobiography



I was born in Lansing, Iowa on June 6, 1918, the third of the four children of William Carl Krebs and Louise Helen (Stegeman) Krebs. My maternal grandmother, Bertha Stegeman, lived with us for most of her life. My father was a Presbyterian minister, who had started his ministry in the Moravian Church in Wisconsin. My mother taught school until she was married. (She must have been an excellent student because she could still help me with problems during my second course of algebra.) As was common in ministers' families, we moved several times, first to Newton, Illinois and later, when I was age 6, to Greenville, Illinois. The family stayed in Greenville, which I always think of as my "home town", until I was fifteen. Greenville is a small college town, has good schools, and is surrounded by pleasant countryside where I loved to go on walks with my older brothers - as soon as I became old enough that they didn't mind having me tag along. In addition to hiking, other recreational pursuits included sand-lot sports, fishing, stamp collecting, and eventually ham radio. The last hobby was picked up not so much because of any strong scientific interests on my part in radio theory but rather from a desire to be able to talk to a grade school playmate who had moved to Chicago. I loved to read - mostly historical novels about the Civil War, the settling of the West, and related adventure stories. I worked hard at school in order to succeed, but I cannot claim to have been a highly intellectual child. I liked to make gun powder using materials purchased from the local drug store or taken from my older brother's chemistry set, but I had no childhood aspirations of becoming a chemist. The closest that I came to expressing an interest in biology was the maintaining of a balanced aquarium.

At the end of my first year in high school my father died suddenly. I was fifteen and was strongly influenced by this unexpected event. Although I had never aspired to follow in his footsteps and become a minister, I had great affection for him and admired the skill that he had in some of his avocations such as carpentry and gardening. My mother was deeply affected by Dad's death, but after recovering from the initial shock began making major decisions mostly centered around providing advanced educational opportunities for her children. It was determined that the family, which had very limited income (It was 1933.), would move to Urbana, Illinois, where my two older brothers were already enrolled at the University of Illinois. There we rented a large enough house so that we could rent out a room to help with expenses. Everyone got some kind of

part-time job. The planning for these changes involved the entire family and without doubt had a maturing influence on both of my brothers and certainly had one on me.

In the period from 1933 to 1940 in Urbana I completed the last three years of high school and carried out undergraduate work at the University of Illinois. Urbana High School was an excellent institution with highly dedicated teachers and a broad range of extracurricular activities that were useful in helping me make up my mind as to what I wanted to do in life. This problem was one that was occupying my mind increasingly at this time. Because these were depression years, my thinking about various professions was colored by the question of whether or not a given choice of work was one in which I could earn a livelihood. I gravitated toward a scientific career, not because of deep interest in the challenges of the unknown, but because I felt that there was security in becoming a scientist. Science courses, more than the others, provided subject matter that I felt could actually be used. These feelings were strongly reinforced by the success of my older brother in obtaining an excellent position after obtaining a Ph.D. in chemical engineering in the mid 1930s. Medicine, as an applied science, was also appealing and offered the advantage of being directly concerned with people.

In 1936, I entered the University of Illinois with the idea of majoring in some branch of science related to chemistry, but I did not have a very clear idea of where I was headed. Taking advantage of an "individual curriculum" program that was available to those with reasonably good scholastic records - and for this reason presumably knew where they were going - I was relieved of the necessity of meeting many specific requirements and could pick and choose courses that I wanted. In this way I was able to take enough biology to meet premedical requirements but could also take the math, chemistry, and physics courses designed for professionals in these fields. By the beginning of my fourth year in college, I had narrowed my choices either to getting an advanced degree in organic chemistry or going to medical school. For the latter financial help would be required. This became available in the form of a scholarship to attend Washington University School of Medicine in St. Louis. At this point I assumed that the agony of indecision was over and my future was now defined. I would become a physician.

During my fourth year at the University of Illinois I carried out undergraduate research in organic chemistry and found it to be a fascinating experience. This was probably the first time that I had ever taken a "course" that seemed like fun. Because I was ahead in my credits, I was able to spend virtually unlimited time in the laboratory. My mentors were Harold Snyder and Charles Price, and to them I will always be grateful for having introduced me to research. Another influential teacher during this period was Carl S. Marvel. Had this research experience come earlier in my college career, I might well have opted for a Ph.D. in organic chemistry rather than going to medical school. But as it turned out, this introduction to research influenced my medical training and without doubt was a strong factor in my eventually becoming a research biochemist rather than a clinician.

Washington University School of Medicine proved to be an excellent choice as a place where I could receive classical medical training but at the same time learn to appreciate "medical research." The basic science courses were the equivalent of graduate courses and there was no attempt to water down the curriculum based on the idea that physicians only need "core"

knowledge in the various sciences. In addition to basic course work that took us to the fringes of knowledge in the various disciplines, students were encouraged to participate in laboratory projects. I personally undertook several projects, first under Dean Philip A. Schafer, who was also chairman of the Department of Biochemistry, and later under Arda A. Green, a faculty member associated with Dr. Carl and Gerty Cori. Ethel Ronzoni also offered me help and advice in some of the work that I carried out. During this period I first heard about the enzyme, phosphorylase, which was crystallized by Arda Green and the Coris and was found to exist in two interconvertible forms that they referred to as phosphorylase b and phosphorylase a. Phosphorylase b required 5'-AMP for enzymic activity whereas phosphorylase a was active without this nucleotide. This enzyme was later to play an important part in my life.

The medical school years, 1940-1943, were war years, and although I did some research as a medical student, my main preoccupation was with becoming a physician who could serve in the armed forces. Nobody knew how long the war would last and our immediate concerns were with being a part of the war effort. After graduation from medical school I had eighteen months of residency training in internal medicine at Barnes Hospital in St. Louis, and then went on active duty as a medical officer in the navy. The war ended and so did the period of my life in which I actively used my medical training in any practical sense. I believe I would have been happy practicing medicine but this was not to be.

After being discharged from the Navy in 1946, I returned to St. Louis with the idea of continuing residency and becoming an academic internist. However, it immediately became apparent that I would have to wait my turn to get back into hospital work, and I was advised by my professor of medicine, Dr. W. B. Wood, to study in a basic science department during the interim. Because of my background in chemistry, I chose biochemistry for this and was fortunate in being accepted by Dr. Carl and Gerty Cori as a postdoctoral fellow. After two years in their laboratory, during which time I studied the interaction of protamine with rabbit muscle phosphorylase, I became so enamored with biochemistry that I decided to remain in that field rather than returning to internal medicine. Again, I had found laboratory experience to be very satisfying just as it had been when I was a senior in college.

While I was on active duty in the navy, my ship had put into Seattle, and I had been impressed by the beauty of the city. So in 1948, when I had an opportunity to go there as an assistant professor of biochemistry, I jumped at the chance. Because I was quite uncertain of my ability to succeed in biochemistry, however, I made certain that I was duly licensed and registered in the State of Washington, so that if worse came to worse I could always "hang out my shingle." Happily, things seemed to go along reasonably well, and I did not find it necessary to use this insurance policy.

In 1950, Hans Neurath became the first permanent chairman of the Department of Biochemistry at the University of Washington and began to build what was to become one of the major departments in the country. The emphasis in the department was on protein chemistry and enzymology, and this provided an excellent environment in which to develop and pursue a research field. I had been in Seattle for five years when Ed Fischer joined the Department. Ed had had experience with potato phosphorylase during his graduate student days and, as indicated

earlier, I had become acquainted with mammalian skeletal muscle phosphorylase in St. Louis. Together we decided to see whether or not we could determine the mechanism by which 5'-AMP served as an activator of phosphorylase b. We didn't solve that problem, but in the course of trying we discovered the molecular mechanism by which interconversion of the two forms of phosphorylase takes place; namely, reversible protein phosphorylation. Similar work was being carried out on liver phosphorylase at approximately the same time in the laboratory of Earl Sutherland who discovered cyclic AMP, the second messenger of hormone action, which he showed was involved in phosphorylase a formation. A number of years were to elapse before it became apparent that reversible protein phosphorylation is a general process affecting countless cellular proteins.

During the early years of our work on protein phosphorylation, Ed Fischer and I worked together very closely even to the point that if one had to leave to give a lecture the other could carry on the experiment of the day. Later, as the field developed we each concentrated on our own specific areas related to the central problem. One of my own projects was concerned with the molecular mechanism of action of cyclic AMP in promoting the phosphorylase b to a reaction. This was eventually solved with the finding of the cyclic AMP-dependent protein kinase by one of my postdoctoral fellows, Donal A. Walsh. This discovery occurred just prior to my leaving the University of Washington in 1968.

In addition to the motivation provided by my research, I was also motivated by interests in teaching and various aspects of administration. These interests led to a desire on my part to become a departmental chairman, and I was attracted by the opportunity that presented itself at the University of California in Davis where a new medical school was taking shape in the late 1960's. I went there in 1968 as the founding chairman of the Department of Biological Chemistry and stayed for a period of eight years. In 1977, however, I returned to the University of Washington as Chairman of the Department of Pharmacology. In each place, I viewed the principal role of the chairman to be the selection of good faculty members, and I feel proud of the results of my efforts in each place. Other aspects of these chairmanships were also rewarding, particularly the opportunity to interact with colleagues in the development of the respective institutions.

An important part of this autobiographical sketch, which I have saved for the end, concerns my family. During my residency years at Barnes Hospital I met my wife, Deedy, who was a student nurse at Washington University. We were married in 1945 shortly before I left to serve in the Navy. We had three children, Sally, Robert, and Martha and now have five grandchildren. After completing her degree in nursing my wife gave up her own career, but she has been a constant and important source of support for me in my own. We shared in the major decisions of our lives, and I feel that I owe her very much, not only for her constant help in my career but also in keeping me aware that there are other important aspects of life.

Edwin G. Krebs died on 21 December, 2009.