

Medicine becomes life-long career choice

By David W. Talmage, MD, FAAAAI

I was born and raised by missionary parents in Korea where I lived until graduation from high school in 1937. I attended and graduated from Davidson College in North Carolina in 1941. At that time I was very interested in physics, but medicine seemed a more socially responsible field. So I applied for the Jackson-Johnson scholarship at Washington University Medical School and received it. It paid all my tuition and fees for four years. I can remember hitch hiking from Davidson to St. Louis.

I ended up in a dormitory on the Health Science campus in St. Louis, rooming with Alexander Ling who had just come from China. He had been accepted into the medical school at Stanford while he was in Shanghai, but his letter telling them he was coming never arrived at Stanford. The Japanese had occupied Shanghai and the mail was lost in the confusion. When Alex showed up in the fall of 1941, they told him their class was already full, but they would try to find him a spot somewhere else. That's how he ended up as my roommate. Neither of us had any money and we cooked rice in our dormitory room over a hot plate. Alex became a successful neurosurgeon in Cleveland.

I had a Sunday job busing dishes at the Golden Fried Chicken Restaurant on Delmar Avenue. I was there on December 7, 1941, when I learned that the Japanese had bombed Pearl Harbor. This was especially ominous to me, because my parents were still in Korea and what would happen to them nobody knew. It was also unclear whether I could expect any more financial support. Government backed loans were unheard of at that time. The week after Pearl Harbor I secured a night job at the City Sanitarium on Arsenal Street. I worked from midnight until 6 am every night, on a hospital ward at the sanitarium. Most of the inmates were asleep. So I had plenty of time to study. My routine was to sleep from 6 to 12 p.m. and from 6-7 a.m. It's amazing what the human body can adjust to. Still I had a reputation for sleeping in class when the lecture was boring. But I'm not sure my sleep schedule had anything to do with that.

Soon after the war started our whole class was inducted into the Army. We were allowed to finish medical school, but we went on an accelerated program that gave us our MD in three years.

After graduation from medical school, I took a nine month rotating internship at the Georgia Baptist Hospital in Atlanta. The main reason for selecting this hospital was that I hadn't yet decided where I wanted to go with my life; so a rotating internship made good sense, and the Georgia Baptist Hospital had a small apartment house for house staff. This was especially convenient because LaVern and I had married three months before I completed Medical School. The war in Europe ended just before I finished the internship and we were assigned to an army base in Columbia, SC, where there were a large number of German POW's. I was able to brush up on my German quite a bit. I remember one of the POWs told me that Russia and the United States would be at war within 25 years. He came close to being right, but it was China not Russia we fought with in Korea.

The war ended in Japan while we were in Columbia and we were immediately shipped off to a Medical Doctors' training school in Carlisle, PA. We were supposed to be there for eight weeks, but half way through the army changed its mind again and sent me down to a base in Longview, Texas where we stayed for a couple of months. I was then transferred to an overseas staging area at a base in Kearns, UT, and eventually to a camp outside Manila on the famous Bataan Peninsula. But it was hot there and there was nothing to do; so I immediately volunteered to go to Korea, where I heard they were having a bad cholera epidemic.

Within a few weeks I was assigned to a camp in Kunsan, on the west coast of South Korea. Within a few months the cholera epidemic subsided, partly due to our efforts of urging everyone to boil their water before drinking it, but largely due to the fact that in the cooler weather, Koreans tend to drink hot tea or the boiled rice water. We spent the winter of 1946-47 in Kunsan where I was the medical officer for a battalion stationed there. I remember one incident at the Army Camp when one of the 18 year old privates fell asleep on his watch and was in a lot of trouble. I was able to find some medical excuse for his failure, and this put me in good with the whole battalion. At Christmas time, they brought us a Christmas tree and helped us decorate it and they saw to it that we were given an opportunity to buy scarce stuff when it was available in the PX. The Koreans saw to it that we had chickens and eggs and we helped some of the local Christians start an orphanage. So all in all

we had a good time in Kunsan. In the spring of 1947 I was transferred to the Provincial Capital of Chonju, where as Medical officer for the Province I was in charge of advising the Korean Head of Public Health for the Province.

When we came back to St. Louis in the spring of 1948, I found a temporary job at the medical school in the department of Preventive Medicine, and after our first baby was born (April 14, 1948), named Janet Lynn, we found an apartment on Yale Avenue not far from the southwest corner of Forrest Park. Just by chance we found that the couple living next door to us in the same department complex was Frank and Marion Dixon, who just happened to have a new baby girl named Janet Wynn. We became good friends. In July, 1948, I began one year of a straight medical internship.

After the internship was completed, I took a fellowship with Frank Dixon in the Department of Pathology. Frank had had training in the use of radioisotopes in medical research and I learned how to use radioactive iodine (I^{131}). Everything had to be done behind lead brick shields because we were using mc amounts of radioactivity. We would first attach the label to a bovine serum protein, either albumin or globulin, add a large amount of cold potassium iodide and dialyze the mixture against tap water to remove the free isotope. I may be mistaken about this, but I don't think we had any way of disposing the waste radioactivity and most of it went down the drain into the St. Louis sewer.

The labeled protein was then injected intravenously into 60 or more rabbits, and we had to bleed them by the ear vein at periodic intervals. After a year of doing this, Frank took a position as chairman of the Pathology Department at the University of Pittsburgh and we went with him to Pittsburgh. My two years with **Frank Dixon, MD, FAAAAI** were a very good training experience. I learned how to do research and to use radioactive isotopes. My own style was different from his because I was more interested in theory and preferred a less hectic experimental life. Nevertheless I learned the ropes of academic life, how to write a grant and write a paper. The work we did on the effect of radiation on the immune response had a lot to do with focusing our attention on the cells that made antibodies. Then by using radioactively labeled antigens I was able to show that there was a great diversity in antibodies and that they were not the homogeneous proteins that the serologists like Kabat and Heidelberger thought.

In 1952 I received an offer from the University of Chicago to come head up their Allergy Division. We decided to go but before we went our second daughter, Marilyn was born on March 4, 1952. I stayed at the University of Chicago for seven years (1952-59). A lot happened during that time. David was born the next April 19, 1953. I developed a close relationship with Dr. William Taliaferro, who was head of the Microbiology and Immunology Department. For several years we had lunch together in his office once a week and discussed the state of immunology. Tolly, as he was called, had a severe allergy to animal dander, and did not go in the laboratory. He left the management of the lab to his wife, Lucy, who was a great organizer.

Tolly would plan the experiments and Lucy would see that they were carried out with great precision. We did a few experiments together. One I particularly remember involved feeding rabbits a yeast hydrolysate that had been labeled with radioactive sulfur (S^{35}), which is attached to the two sulfur containing amino acids. Some of the animals had been immunized and when their spleen cells were transferred to other naive (un-immunized) rabbits, then the animals receiving these cells made antibody which could be detected in their blood. If the radioactivity was given to the immunized donors of spleen cells, then the antibody made in the recipients was not labeled. But if the radioactivity was given to the recipients, the antibody was labeled. This convinced us that the spleen cells contained the machinery for making antibodies, and were not just reservoirs of preformed antibody that was released in the recipient. This was important because there were some immunologists that had speculated that immunological memory was just the release of preformed antibody. These and other experiments we did convinced me that the memory lay in the expansion of the antibody forming machinery.

Other experiments I did in my own laboratory involved the use of radioactively labeled antibody and the newly available I^{125} from Oak Ridge. We also had one of the first well counters from Texas Instrument Co., which could detect gamma rays in liquid solution in test tubes. This avoided the copper planchets which we had used previously to detect beta rays from dried samples. This increased the pace of research tremendously. I^{125} has a much weaker gamma ray than the I^{131} used previously and could be used more easily because of the reduced risk.

Using these new techniques I was able to absorb labeled antibody on to antigen attached to cellulose columns and determine how firmly the labeled antibody was bound to the column. I found that there was tremendous diversity in the strength of these bonds. Some of the antibody could be removed from the column with saline washes, others could be removed by

exchange with unlabeled antibody, and some was so tightly bound that it could only be removed by acid solutions. I also found that antibody could be separated into different fractions with salt precipitation techniques. Some of the antibody was the so-called macroglobulin with a molecular weight near one million, while other antibody was regular gamma globulin with a molecular weight around 150,000.

Both the experiments that I did with Taliaferro and those in my own laboratory convinced me that antibodies were natural proteins made according to information contained in the inherited genome. It was just at this time, 1953, that two important discoveries were made. One was the determination of the structure of DNA by Watson and Crick, and the other was the discovery of acquired immunological tolerance by Billingham, Brent and Medawar. In 1955, Jerne published a paper proposing that antibodies were made by a process he called "natural selection." But the mechanism of selection that he proposed was that a natural globulin or "antibody" was selected by antigen, then absorbed by an antibody producing cell, which then made millions of copies of this protein. According to Jerne's theory the sequence of amino acids in a protein was determined by copying the sequence of an existing protein. This was contrary to the idea that was becoming popular at that time, namely that the information for making protein was in the DNA. Thus, it was not difficult to develop the idea that the diverse globulins that different cells made were based on some differences in their DNA. That was the origin of the cell selection theory.

I finished the paper proposing cell selection during the Christmas Holidays of 1956 and sent it off to the Annual Review of Medicine. I also sent a copy to Sir MacFarlane Burnet. This was very fortunate because he refers to this preprint three times in his own paper published in 1957 in the Australian Journal of Medicine. In subsequent papers on the "Clonal Selection Theory," which Burnet published he never gave me any credit.

During the winter of 1957-58 we spent three months on sabbatical at Cal Tech in Pasadena, where I worked with Dan Campbell and met **Kimishige Ishizaka, MD, FAAAAI**, and **Teruko Ishizaka, MD, FAAAAI**. Dan could never accept the selection theories of antibody formation, but he had a very congenial personality and we always had a good time arguing about it. It was at Cal Tech that I heard about Jenne's Natural Selection Theory. He had been at Cal Tech a couple of years earlier.

In 1959 we moved to Denver to take a job in the Department of Medicine as head of the Allergy Program at the University of Colorado School of Medicine. I have served the University in many capacities since 1959. The first four years I was in charge of the allergy program. It was during this time that **Henry N. Claman, MD, FAAAAI** joined the group. Joe Ingraham joined us for a year on sabbatical from Indiana, and Andor Szentivanyi, MD had come with me from Chicago. It was during this time that Claman developed his technique of transferring thymus and bone marrow cells to radiated mice, which eventually led to the discovery of collaboration between B cells (bone marrow) and T cells (thymus). Szentivanyi was working on his theory of beta adrenergic blockade and Joe was working on his gel culture method of identifying and counting the number of antibody forming cells in the spleen and lymph nodes. **David S. Pearlman, MD, FAAAAI** and Vince Fulginiti also worked in the lab for a while. It was a very active and exciting time in immunology.

From 1966 to 1971 I was in the Dean's office, two years, as Associate Dean, one year as Acting Dean and two years as Dean. After leaving the Dean's office I had the good fortune of collaborating with Kevin Lafferty in Australia. He spent a year's sabbatical in my lab and I spent a few months in Canberra.

My curriculum vitae has details on all the other jobs I have held at the University and the papers I have written. Currently (2005) I am volunteering on the Admissions Committee and the Human Research Committee (IRB). We were blessed with two more children, Mark in 1959 and Carol in 1961.