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Reminiscences

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Taking into consideration that the doctors are very often enchanted by poetry and literature, and sometimes they even create one themselves, we have decided to publish in this column as a sequence in a few following issues, the autobiographic literary works of Prof. Dr Rajko Igić.

My career in medicine and research spans many decades. Although I owe much to various collaborators and mentors, I am especially indebted to Dr. Ervin G. Erdős. This exceptional man and scientist not only brought me to this country, but he helped me to realize a number of dreams and ambitions. Thus, I offer a special tribute to Dr Erdős for his continuing interest in me, my family and my work.

First International Conference

I first met Dr. Erdős in June of 1969 at the International Congress of Pharmacology in Basel, Switzerland. I had come from Dubrovnik with a small group of associates from the Institute of Pharmacology in Sarajevo. All of us who came to present our work were young and enthusiastic with many expectations for the future. It was an excellent opportunity to meet the international research community and to exchange ideas with fellow scientists from all over the world.

Our small group from Sarajevo first attended a workshop in Kotor organized by the International Brain Research Organization, an institution, founded by researchers from Belgrade and Los Angeles to unite scientists from two separate military blocks and the unaligned countries. For an entire week we heard famous neurophysiologists and neuropharmacologists-scientists from Moscow, New York, Prague, Chicago, London - present their research and discuss the implications. All their modern technology for studying electrophysiology of the brain amazed me, but I was most excited by meeting and talking with these outstanding people. I was very honored when one professor invited me to talk about my research at his university in New York. Although I was unable to make such a trip, I was honored to be asked.

From Kotor via Dubrovnik, we then traveled to Basel for the International Congress of

Pharmacology. This was my first exposure to an international congress. I presented a paper on experiments done in Sarajevo on how drugs influence certain behaviors in rats. I am pleased to say that this was well received by the audience.

On the second day of the Congress, Professor Klaus Unna from Chicago invited our group to the most beautiful pastry shop in all of the city of Basel, where a large terrace overhangs the Rhein River. Professor Unna was well acquainted with our professor, Paul Stern, who was kind enough to introduce us to his friends and colleagues. In addition to the stimulating conversation with that fine gentleman, we were each given a group photograph as a memento of the photo occasion. Although, now it has been many years since we sat together on that terrace in Basel, this reminds me of how eager we were to meet each other and share our stories.

I met Professor Erdős at the final celebratory dinner of the International Congress. I was surprised to find him so young, despite all his achievements. After all, he had published many scientific papers, edited the proceedings of several international symposia, and he was already a well-known professor in the United States. We found much to talk about over dinner, and by the end of the evening, the professor invited me to join him the next day on an outing to Lake Luzern. He rented a car for the trip, and, together with another doctor from the United States, we departed on an excursion that lasted from early morning till night. Along the way we discussed many different subjects, and I was amazed to find that the professor was as well informed about painting, music, history and politics as he was about science.

At some point, Dr. Erdős asked me if I would like to come to Oklahoma for a year as a postdoctoral fellow. I was delighted to receive the invitation, but I explained that, even though I was already a medical doctor, I must defend my Ph.D. thesis before I could leave Sarajevo. I never really believed that it would happen, but two months later I received an official invitation from the University of Oklahoma and all the application forms necessary to obtain an American visa. I was also lucky enough to get a Fulbright travel grant, and after I defended my dissertation early in 1970, I was on my way to Oklahoma.

In Oklahoma

I knew little or nothing of Oklahoma, so I consulted a world atlas in hopes of finding whether it had roads and railways. The atlas provided very little information, but from some source or other I learned that the Indian word "oklahoma" means red earth. I would soon see

this for myself.

Imagine my surprise when I stepped off the plane into a large and thoroughly modern airport! And there were such huge highways-certainly much wider and more extensive than the narrow roads of Sarajevo. I was even more amazed by the time I reached my temporary lodging at the Faculty House. This facility with its olympic swimming pool was far grander than any faculty quarters that I had ever seen in Europe. Oklahoma seemed a paradise indeed!

The laboratory. Professor Erdős ran his research operation from a large, well equipped laboratory in the medical school. This lab was far more active than any of those I had known in Yugoslavia. The research team consisted of several individuals who were dedicated to studies of vasoactive and neuroactive peptides, potent biological mediators of many diverse physiological functions. The professor himself supervised each aspect of the work in this rather specialized environment, meeting and talking with each member of his research team on a daily basis. No experiment was carried out without his supervision.

The democracy of the laboratory atmosphere was an additional surprise. I was unaccustomed to seeing professors and doctors involved in the most menial aspects of laboratory work. For example, in the Oklahoma laboratory, each researcher would go to the animal room, collect his own rats and make all of the required preparations. Professors in Sarajevo never did that. There was always a technician to do the preparations, and the professor would merely supervise. At first I felt deprived of this convenience, but I soon learned the benefits of the hands on approach. I learned many new laboratory techniques and even introduced some new ones (radioimmunoassay, disc electrophoresis, etc.) into the laboratory repertoire.

With time, and with the help of my colleagues, I soon mastered the most important techniques in protein and peptide chemistry. Once I had become sufficiently confident in my own abilities, I approached the professor with the idea of letting me purify an enzyme of key interest to his laboratory. This was the now well-known angiotensin I converting enzyme, which we abbreviate ACE. I wanted to find out whether this particular enzyme could do two completely different things-activate the hypertensive peptide, angiotensin and also inactivate a hypotensive one, bradykinin. Professor Erdős had already described an enzyme that would inactivate bradykinin and he put forth the hypothesis that ACE might be a key enzyme for a more general action in the metabolism of vasoactive peptides. To test we would need an absolutely pure preparation.

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Professor Erdős discouraged me at first. He explained that the purification of ACE would be an arduous task. No one thus far had managed to do it, although many were working on the problem. I refused to be discouraged, and with the collaboration of a small laboratory subgroup, I finally obtained what appear to be a pure product. According to disc electrophoretic criteria, we had only one protein, but we needed to prove that it would do both tasks-inactivate bradykinin by cleaving off the C-terminal dipeptide and also activates angiotensin I to a potent vasopressor substance, also by cleaving a dipeptide. We were able to do so, and thanks to this initial success, I received a two year grant from the American Heart Association to pursue this project further.

Collaborations and friendships. Professor Erdős' laboratory was consistently populated with young researchers from different countries. These people came to spend a year or two in the laboratory to learn the practical, "hands on" approach to basic research. Many came from Japan, and most of the Japanese were so successful that they published 4 or 5 research papers during their brief visit. However, there is always the exception to the rule. Dr Shigetoshi Chiba, a young pharmacologist from Japan, could not get his bearings in our lab. For a time, it looked as if the Professor would have to send him back to Japan before his term was over.

I knew Dr. Chiba well because he lived in my neighbourhood, and we sometimes went bowling or played ping-pong or tennis together. He was also a frequent dinner guest at our home, since he had left his wife behind in Japan. Being aware of his problems in the lab, I suggested to Dr. Chiba to help me develop a radioimmunoassay for angiotensin I. He freely admitted that he was not much interested in that aspect, so I proposed a completely different project—we could study how tremorine and oxotremorine affected the sinus node of the heart. We could apply these substances to an isolated branch of the coronary artery in anesthetized dogs, and because this artery supplies the sinus node, we could then determine how these agents affected the electrophysiology of the heart. I had earlier studied effects of tremorine, so this was a logical continuation of my own research interests.

Once we began these experiments, Dr. Chiba proved himself very capable. We quickly obtained data that were subsequently published in the *Tohoku Journal of Experimental Medicine*. Later Dr. Chiba had a brilliant academic career in Japan, where he became a Chairman of the Department of Pharmacology in Matsumoto, Japan. He eventually published more than 150 papers in peer reviewed journals, and he is presently the Dean of the Medical School. Some years later when I became a department chairman myself, I invited Dr. Chiba to lecture to our students and graduate students in Tuzla. We also formed a collaborative arrangement between our universities which enabled some of

our young doctors to train in Japan.

Among the many visitors to Dr. Erdős' laboratory was an Israeli scientist, Dr. Yehuda Levin, from the Weizman Institute. At one point, my wife returned to Yugoslavia for a visit, and Dr. Levin shared my apartment in Oklahoma City for a month. This interesting, witty man was always in a good mood. He was very fond of music, despite the fact that he could not sing a note, and he didn't play a single musical instrument. Nonetheless, he knew several entire operas by heart.

Yehuda and I agreed to share kitchen duties and to alternate in the preparation of meals. If I did the cooking, he would wash up, and vice versa. Yehuda was the master of leftovers. He taught me to cook much more than we needed for a single meal so that we would have leftover ingredients for soups and other concoctions. I frequently prepared various dishes from Vojvodina, going by memory of what they contained. Yehuda would counter by cooking Israeli foods. It made for an interesting blend of culinary cultures.

Once I planned to make a particular soup that required a nice piece of beef and a beef bone. However, at the local supermarket I couldn't recognize meat cut in the same way that I knew in Yugoslavia. Eventually, I settled on some pieces that were wrapped in plastic. When Yehuda inspected my purchases he laughed at me, saying "But it is for barbecued steaks!" "We will use it anyhow", I said. I prepared my soup, and it was actually very good. Yehuda and the others in the laboratory teased me about this culinary triumph, now referred to as "steak soup". I then resolved to write down my favorite recipes. Later I shall relate how I achieved fame as a chef in Dallas, Texas, where people have more refined taste than in Oklahoma.

American impression. During my two-year stay in America, I learned many different things. Not only did I learn the modern and efficient laboratory methods that were part of my job, but I discovered that many things outside of the laboratory that I could take home to my country. Realizing that I would need to remember a lot of details, I bought a large notebook to record impressions and ideas. I was particularly interested in urban architecture and in the structure of roads. In America even the smallest alleys were wide enough for cars to maneuver around each other and to turn around. In my homeland, where streets are generally narrow and closed, the end of each alley should be broadened to permit cars to turn around.

I recorded a number of notable differences between America and Yugoslavia, including such things as handicapped accessibility to public places and general concerns with public health problems. In Yugoslavia, builders rarely design entrances to public buildings, trains or buses for handicapped persons, but handicapped access is a regular (and required) feature of public facilities in America. Thus, disabled

people in America are quite independent. They do not depend as much upon the help of others as their counterparts in Yugoslavia, and they can accomplish much more in terms of daily living.

I know personally an American medical doctor who had paralytic polio when he was a student. Although he was confined to a wheelchair, he was able to complete his studies, and, after graduation, he became a famous anesthesiologist and researcher. In contrast, the university administration in Tuzla once refused to accept a medical school candidate who lacked one finger.

I could note help but not that Americans enjoy much greater overall health than the citizens of my own country. I wondered, what factors enable Americans to stay healthier and live longer than most Yugoslavs? One factor is certainly that in America most people take an active interest in every advancement of medicine. The Americans are surprisingly well informed about the need for healthy diets, regular physical activity, and about the dangers of smoking. Not all adhere to the recommended guidelines, of course, but they remain well informed.

Our first son, Petar-Gordan, was born in Oklahoma, which further strengthened our family's ties to the United States. Although I had begun to feel quite at home in Oklahoma City, it would soon be time to return to Sarajevo. Professor Erdős donated many supplies for my laboratory back home so that we could continue our collaborative work. I also bought a number of textbooks and some small pieces of laboratory equipment which I packed into 10 boxes and a large chest. All in all, I returned to Sarajevo with many more gifts for my laboratory than souvenirs or things of personal use.