NIDDK
Oral History Project
Interview with Dr. Paul Kovac
Conducted on April 22, 2019 by Kenneth Durr

KD: This is an interview with Dr. Paul Kovac, Chief of the Carbohydrate Section, Laboratory of Bioorganic Chemistry at the National Institute of Diabetes and Digestive and Kidney Diseases. Dr. Kovac, thank you for taking some time to talk today.

PK: You're welcome.

KD: I want to start with a little bit of background and your background is particularly interesting, so I want to go back to your childhood and just talk about growing up, your father and circumstances.

PK: I grew up in former Czechoslovakia. My father was a college professor. It was an agriculture college. My mother was a home keeper and my father was a scientist, but he had nothing to do or not much to do with chemistry, but only as much as agriculture required.

KD: He was a chemist?

PK: Not really. He wasn't a chemist and I never thought that I would become a chemist or a scientist. That was a completely foreign to me. I was a regular kid, kicking balls the same as others. I was bicycling and going swimming. And what I find not quite in line with my

becoming later a scientist that I was a very average student. I was, in mathematics, a below average student. I didn't have much interest in school or studying. I remember that my parents tried to get me to take piano lessons. That didn't last longer than one year. Up until ninth grade I was an average, mediocre student and can attribute it to not very good teachers. Why I'm saying that is when I went to real high school, everything changed suddenly, like the strike of a magic stick.

In Czechoslovakia there was a very good network of specialized high schools. After junior high, my parents had a choice to have me enrolled into a regular high school where I would be getting general education, or some specialized school where I could become a chemist, an electrical engineer, or architect or something like that. There were also specialized high schools for nurses, which was graduates from those schools were equivalent probably to a bachelor’s degree here.

My father didn't want me to enroll in a regular high school because those were very difficult times in the early '50s in Czechoslovakia. It was only a few years after a change of government from a fully democratic government before 1948, to a communist dictatorship, and people who had an intellectual background were not really in favor. You had to be from a working class to have access to everything and because of my father's few black marks in his file, he didn't believe that I would be able to enter university. So he wanted me, before I would even apply, to have already something in my hands, some professional thing.

I was just a regular kid, very impressionable and I was pretty indoctrinated by the system and I believed in the ideology and I thought that my role would be best fulfilled if I go to the rural areas and become a teacher of the under-privileged children. I wanted to become a teacher of elementary school or something in the remote areas. Well, it didn't fly very well with my father who was a scientist and he said that I should choose from one of those more proper schools where I should get some practical education and that if I wouldn't be able to choose then he would choose for me. I really couldn't choose anything because I wasn't interested very much in these things. The only thing I was interested in, which was more intellectual—I was an avid photographer. I was an amateur photographer. I used to make my prints myself in the basement dark room, which I created in the apartment where we lived, and that had maybe a little bit to do with chemistry, but I didn't look at it from that point of view. I just liked to take pictures and make them, but I didn't think about chemistry.

Because my father was in agriculture and I was interested in photography he thought that maybe chemistry should be the school, so he enrolled me in this high school specialized in chemistry, and I started to prosper very well. And I must say, with a little sarcasm, that I thank my originally becoming a chemist to the communist system. Why am I saying that? Because our teachers were qualified, the best teachers from the universities, and they were not allowed to teach at the universities because of their background and because they were bourgeois. So these technical high schools, they usually had excellent teachers.

KD: Did you get into organic chemistry at that point?

PK: No. The first studies were general chemistry and it was excellent, and then we couldn't choose the subjects or the field that we want to expand on our knowledge in chemistry. There were eight graduating classes in the school where I went to and they simply said, from A to Z, there would be food chemistry, there would be organic chemistry, so I became an inorganically trained chemist. But what is important is that we got excellent in basics, so we could then later build on those very good basics. I think it was a fantastic school because, as I only later realized, the knowledge which we acquired was lasting knowledge. Unlike graduates now days, these young people who I meet here, I discovered that even though they had basics, those basics evaporated five minutes after they passed the exam, and our knowledge was pretty lasting.

KD: How did you go from that high school to Slovak Technical University?

PK: That's also interesting. I always knew my way with words because I was an avid reader. We had a school newspaper at that high school and I was on the editorial board of the newspaper. And as some stupid prank, we wrote some articles in the newspaper which were not really favored, which described the staff, and that was a big no-no because discipline was very strict. So as a punishment, the director of the school cancelled the prompts, and this was six months before I was supposed to graduate. Another punishment was that the editorial board, not only did they not recommend for university, but they couldn't even apply to university.

So I was supposed to, after graduation, go into industry and it was an assigned place and there was no discussion about it, you have to go there. Maybe later you can change employment, but at the beginning every graduate was assigned a place where he had to go, and it was the same thing when everybody graduated from university. So because I was not allowed to even apply to enter university there was, again, the question, what am I going to go. Even though I had a place in the industry assigned, my father, with his connections, arranged that I went to work in a small city about 80 kilometers from where I grew up, in a dairy factory, because he knew somebody there, and he already prearranged that after some time the industry would recommend me to go to the university. This is how the system could be outsmarted somehow.

I entered the factory and I was working at quality control as a chemist and I learned something about how to make yogurt and all kinds of requirements for fats and minerals. As an organic chemist, I had some background there and I was pretty happy there. Three months later, in September, there were some additional entrance exams at the university, at the Slovak Technical University, and I was already recommended by the industry, so all the black marks from my past were wiped out and I was able to enter the university. This was a five-year establishment, so I studied for five years. And we took also one day a week, military training, which allowed us, after graduation, not to have to go, literally for two years, only for one year because we had some head start and we had some training during the university years.

KD: Did you enroll in the university in the chemistry program?

PK: Yes, this was the chemistry department.

KD: Who was your mentor? Was there someone you studied with?

PK: It was different than here. The system is completely different. You have your classes, no choices of subjects or classes. When I look back, actually it was not bad. I would say that the communist system screwed up many things, but not education. Education was very good. They added some nonsense, some indoctrination, but they didn't take out anything, so we had a very strict regimen of classes which we had to attend. We had our seminars which we had to attend. We had preliminary exams, no multiple choice tests, which ruined every country's educational system, including the U.S. educational system, where you had a 30 percent chance of passing even if you don't open the books. You just guess some of the answers. I can see that's not really a good system. When we went to exams we had to have a written exam first, and only when you passed that you went to an oral exam where you had to coherently talk about subjects for 27 minutes.

KD: Sounds like a graduate program today.

PK: Well I haven't gone through the system. I don't know what the graduate program looks like.

KD: Did you end up with a degree in wood chemistry?

PK: Yes. Eventually I had the choice, the third and fourth year I was pretty free to choose one of the subjects. Even though I was a good student at that time, I was an above average student at that time, I still never thought about becoming a scientist. I knew that I would be working somewhere, but it never really appealed to me to become a scientist.

I graduated and I was assigned a job in a furniture factory as a chemist, as a wood chemist. Wood, makes sense, right? It was a little bit farther from my hometown and I didn't know what to expect, so I borrowed by father's car and took my girlfriend, my present wife, and we went to explore the furniture factory. I met the manager of the lab where I was supposed to work and he said, “Look, we don't need you here, but we cannot release you from the assignment. You have to show up.” So I didn't show up because in the meantime I had to enter the military service. I was supposed to show up after one year.

I did my boot camp and I started my training and everything. I hated every minute of it, really. That was not something—because there was discipline there and that didn’t go very well with me. But I thought I would stick it out and I would survive it, and everything would be fine. This was 1962, winter of 1962. I remember those days, not many are alive anymore because it was a long time ago. This was the time of the Cuban Crisis and the system was very paranoid, like tomorrow somebody is going to invade us or we will have to help Cuba. So they immediately increased military service for another year, no questions asked, no exceptions. That's what I thought. And I already panicked: what am I going to do there for two years?

Occasionally, we could go home for a weekend. One day I went home to my hometown and met one of my past classmates and we exchanged experiences from military service, and the topic of extending the extended service for one more year came up. And he said, "Haven't you heard about this little regulation which says that if you enter grad school you don't have to serve that one more year?" So even though I never thought of going to grad school that was a pretty good incentive and I applied. I brought some books to the barracks and did some reading, some refreshing, and I passed the exams. And come next September 1, I entered grad school at the Slovak Academy of Sciences. Again, I can thank my fate to the communist system which first extended this for one year and then put a little back door how I could get out. And I really loved it.

KD: How soon did you plan a thesis? When did you decide what you would study?

PK: That was assigned. I had a degree in wood chemistry from university, so something in wood chemistry would make sense. And I became a member of a department at the Slovak Academy Sciences in the Institute of Chemistry where they were studying wood polysaccharides, so I studied polysaccharide chemistry. There were many dramatic things which happened during my grad school. I was working on my thesis, which consisted in the first year only of some classes, no lab work the first year. We had to choose one foreign language in addition to the compulsory Russian, and I chose German. Why German? Because my hometown was only three kilometers from the Austrian border and I grew up on Viennese television, so I wanted to improve my German. I picked up

German first from television, actually. It was a very fortunate geographical situation when in the morning we were pumped with some propaganda, but when we came home in the evening, everybody opened the radio or TV and we had the real news and also entertainment, so I was interested in improving my German.

I started taking some English classes only about one year before the graduation when I needed more to study some literature for my work. And I was using the dictionary, and here and there I picked up something by reading. The expert language is usually very simple, much easier than anything else, so I could get by, but I still was taking German as my main foreign language. Why I did start more intensely to be interested in English was because about one year before I was supposed to submit my thesis and started writing my thesis, my director called me to his office and asked me if I would consider after getting my degree to go for post-doctoral training to the United States. This was 1967 when there was a political thaw in Eastern Europe. Everything became a little freer. Before that it was unthinkable to go to the West Country even for vacation. And this suddenly came up as a possibility, so I of course was very happy that I was offered that. And it was only because he knew somebody in the United States, who wrote him a letter that he has a position in wood chemistry and if the director had somebody on his staff who would be suitable for that position. So that's when I saw the vision of maybe going to the United States, I started taking private lessons in English and I started to read more in English, and this is how I came to the United States.

KD: Was that Roy Whistler?

PK: That was Roy Whistler, yes. Roy Whistler was a very good man. I think he was very friendly from the beginning because he was a travelled man. So he actually visited my institute before and that's how he became friends with my director. But other people at the university, when I showed up, they thought I was from a different planet. I was an exotic element there, everybody thought I had maybe one more pair of eyes and maybe two noses on my face. I came from the communist world.

KD: You were at Purdue?

PK: Yes and it's the Midwest and mostly conservative. But it took maybe a week or two and then I'm just like everybody else, except that I don't speak English so well. But otherwise, they were very friendly and helpful, and I formed very good friendships and I have corresponded with them for a long time. Actually, there was a post-grad there from Japan who I still now exchange Christmas cards. It was my best time of my life even up to now, when I was there. The country was different and the university was fabulous.

KD: Your post-doc was going to be in wood chemistry.

PK: Yes.

KD: Did you start expanding your horizons more on what you wanted to study?

PK: Well I was assigned my project and I was very happy that the project was very close to what I was doing with my thesis, because my greatest fears before I went, were that I wouldn't qualify for the job. I didn't know what to expect and what they expected of me, but fortunately I was assigned a project which was very close to my thesis. I knew the equipment necessary, I knew the methodology. I encountered new things, and that was a good thing. I learned a lot, of course. But the next lab, it was not wood chemistry, it was something else. It was synthetic carbohydrate chemistry.

KD: Was this still at Purdue?

PK: No longer because Whistler was dead and the department had some different interests. I don't know very much about what's going on there because I never visited Purdue University after that. But what was interesting for me and for my career is that in the next lab there was this synthetic organic chemistry, carbohydrate chemistry, that was being pursued. That was a very interesting time for carbohydrate chemistry because thiosugars—which are carbohydrates where instead of oxygen in the ring there are other atoms, among them sulfur—were a very big thing at that time and Whistler's lab was very big in thiosugars. Actually they published and patented the first male contraceptive where thioglucose was part of the drug which they tried to bring to the market, which was working already on small laboratory animals as a male contraceptive, and that was supposed to be a big thing. So they were extensively doing this chemistry. And I was just looking and it became interesting.

I made friends with Whistler's most senior post-doctorate fellow, Dr. Nayak from India, who was an excellent chemist, excellent carbohydrate chemist and excellent teacher. I approached him once and asked him if he would take me at night and weekends as an apprentice, and he said he would have to ask Whistler, and Whistler didn't mind. So I spent some time with Dr. Nayak, and I became fascinated with this new field, which was completely different than polysaccharide chemistry. I developed such a liking that when I came back to Slovak Academy of Sciences, I asked my director if I could switch fields. And again, I was lucky. He let me do it.

KD: Was this also a post-doc when you came back to Bratislava?

PK: No. I did a staff position. Before I go there, let me just mention that in 1968, which was still my year at Purdue, 1968 was when the Russians came with tanks and occupied a country of 12 million with 600,000 troops and who knows how many tanks and airplanes, and whatever. I was in the United States and I missed that development. And of course, all the mail which I was getting from home was telling me, including from my mother: don't you even think of coming back. My mother was not really in good health and my family was there as hostages. So I first asked for an extension of my exit visa from the Czechoslovak Embassy and I got it only for three months, so I only could stay three more months. And during those three months I still could make some decisions, but all the circumstances dictated that I should go back. As a naive young scientist I thought I would be the good guy, because after the invasion when I had a chance to stay, I didn't.

I came back and the first two or three days were fine, but then I discovered that I was a CIA spy. Of course, with everything forbidden my life as a scientist was actually impossible to live because in science you need communication with the rest of the world to keep abreast with everything. We had a good library, I must say. We had all the books and journals available as illegal copies from China—it was the same *Journal of the American Chemical Society*, except the binding was different. So we could read the literature, but we couldn't correspond with friends, we couldn't attend meetings. My first and the only international meeting I could attend was the one which was held in Czechoslovakia by chance, so it was very bad times.

On top of everything, in 1977, I suddenly got a letter from a Michigan company, Upton Company, a pharmaceutical company. One of the guys was establishing a second carbohydrate journal, international journal, and I got an invitation from him to join the editorial board. That was something which was very unexpected. It was only about six, seven years after getting my degree. I didn't know anybody there. They must have made the choice only because they read what we published during those years. I was ecstatic, of course, but I needed permission from the communist authorities to do that.

I was invited to a meeting of the committee of something and they asked me why I want to be there. I said, “It's not I want to be there, they chose me to be there.” They were again suspicious because probably I will have to travel, even though it didn't require any traveling, but they don't know how science worked. My request was denied. I couldn't do it. I couldn't join the editorial board of a scientific journal. So I went to my director who I

knew was looking at my work favorably because we were productive, and I asked him what to do. I was denied. But he was a wise man and he knew how this political system works. He said, "Don't answer that invitation because if you don't answer it, it will be assumed that you accept it. Who in the world would refuse something like that? And these guys don't read those scientific journals anyway. They will never know." So I went for it and that's what happened. I didn't answer that letter, and when the first issue appeared, my name was there. Of course, I hid it not to get into hands that they would discover it and it was like that until I left.

KD: What were you publishing? You said you didn't have access to the cutting edge of the field, perhaps, but what kind of work were you doing?

PK: At first, at the beginning of my career as a synthetic organic chemist, as a synthetic carbohydrate chemist, I was working on a subject which I chose myself and which I thought would be useful for the institute. When I was working on my thesis on structural research in plant polysaccharides, that required very sophisticated analytical chemistry. We had some good instruments. Well, good for Eastern Europe, it was not quite the best development in the world, but it could do very good work, I think, because if it wasn't, I wouldn't be invited. They wouldn't think by reading what we published it was worth inviting somebody, so it must have been pretty good.

Then when I came here and I realized what is going on here, we were doing some very good synthetic carbohydrate chemistry with synthesizing oligosaccharides. At that time,

oligosaccharide chemistry was not really all that advanced and anything before trisaccharides and tetrasaccharides was a big accomplishment. We were synthesizing pentasaccharides and hexasaccharides, with a rather primitive arsenal of chemicals. I had to synthesize chemicals which here costs pennies and can be ordered and delivered in 24 hours. But we didn't have foreign currency, so we couldn't order it. We had to synthesize our laboratory chemicals, some of them. But this made me a better chemist.

Not only that, the Eastern European world was such where everything is in shortage, starting from toilet paper to sophisticated chemicals. So we were forced to improvise. When we didn't have what we needed we figured out how to do it without the necessities. It comes handy even here sometimes. That was maybe one reason why people who come here, scientists, and stay here, they usually succeed. I consider myself an American success because I came here with a suitcase of dirty underwear and here I am a section chief of the oldest carbohydrate group in the whole world. I must say that I didn't do so poorly.

KD: What was the goal of doing the synthesis?

PK: For the polysaccharide chemistry, using a limited arsenal of instruments, we needed standard materials, standard chemicals, standard derivatives of carbohydrates and those were not available. Only when somebody went abroad and was gifted some of these very precious materials—these were methylated sugars needed for methylation analysis of polysaccharides to elucidate the structure. These methylated sugars were in great demand

and were not easy to get. So my first big project was to synthesize a series of model compounds, methylated sugars for structural research. Then later I started again synthesizing model compounds for polysaccharide chemists, not methylated sugar, but oligosaccharides. I synthesized the oligosaccharides as structural units of structural plant polysaccharides: xylans, galactans, glucans. Other people were working on these structures and they needed them, and that's why the Institute supported this kind of work because it was useful for other people at the Institute.

KD: You were making the building blocks.

PK: Yes, I was making these building blocks. It was good training in the manipulation of structures of carbohydrates and transferring one to the other, and making all sorts of useful derivatives, which tremendously helped me when I came here.

We synthesized and published syntheses of these very sophisticated structures and this drew attention of the carbohydrate world to our work. I remember, in 1974 when there was this international meeting held in Czechoslovakia, many people who came from the U.S. and Europe, and elsewhere, they came to see me because they knew our work. I was so flattered and I formed some very good friendships from those days with foreign scientists.

KD: You were a young scientist yourself, at that point.

PK: Yes. I was 35, 37. I came here, I was 43 when I came here. So that was something. Everybody was very surprised back home when they learned that at this age I ventured to emigrate illegally and start a completely new life. I was surprised myself, but they made my life so miserable. Again, I thank the communist regime that I am here, because had they not made my life so miserable over there I would never think about coming here.

KD: How did you get here? What was the decision?

PK: I landed in California, but before I landed in California, again, because I was not allowed to travel anywhere and my life as a scientist was limited by that, I decided that I will use my first opportunity and I will try to emigrate. I didn't really know exactly where, but my first choice was the United States because I was already here once. I knew the system, I spoke reasonable English, and that was my first country of choice. My wife has two sisters in Austria, married to Austrians, so we were allowed to visit, and we visited and never came back. Actually, we didn't even leave the country, all three of us together, because that would be maybe suspicious. So we didn't even leave from the same border crossing. My wife stayed behind for a week or two and I with my son left, and then later, she crossed the border illegally with her exit visa for three weeks, same as ours, through a different border crossing. That was the time before computers, so we didn't match up and that's how we were able to leave and not get caught or shot at the border. We didn't really literally jump the fence, but we left illegally.

Then we approached a refugee organization in Austria and they sent us for three weeks to sort of a camp in Italy. And because I had a second cousin in the United States, we got an affidavit of support and it happened that we spent in the refugee camp only six weeks, unlike for some people who stayed there for a year or two, because if you don't have a sponsor it's not so easy.

KD: What year was this?

PK: 1981.

KD: You flew to the United States then?

KD: I flew to the United States. I was alone. I paid for three tickets and it took about two or three years, but I repaid every penny of it. And when we landed I didn't get one penny of government support because for those first few weeks I stayed with my cousin and I found employment in California with a small chemical company, Bachem Incorporated in Torrance, where I was assigned the work to establish a new product line. I was a carbohydrate chemist, and nucleotides and nucleosides are partially carbohydrates, so that's why I was considered for employment, but I never even touched or synthesized, or read much about nucleosides, so I was a bit scared. They were very nice and they sent me for some initial training in this kind of chemistry to City of Hope in Duarte, California. There was a big research institute where they were doing this kind of work, so I was

commuting 70 miles from Los Angeles to Duarte and I joined a group for some time which was involved in oligonucleotides and oligonucleosides.

I was familiar with the chemistry and everything went very well, so after three months I started working in the lab, which was actually an empty room. I had to order all the equipment and establish the lab. I got one technician working with me and we started doing essentially the same work as I was doing in Duarte, California. But to scale up this chemistry took much more than making a bigger pot and we were sweating blood. It was very difficult. I was a little arrogant and thought if I can make oligosaccharides, which is not easy chemistry, I can do anything. It was not like that. Thousands of dollars went down the drain before we developed our own system to do this kind of chemistry on a large scale.

KD: Why did Bachem want large quantities of oligonucleotides?

KV: That was a new field. Machine synthesis of DNA was just starting and there was one company, I don't remember the name of the company, that was making this and they were the second company who wanted to get into this field. And when we eventually learned how to really make these compounds on a large scale they were making tons of money because these compounds are needed for research in milligram quantities, and we were making these 30 grams a day, and they were selling them $1000 a gram. So two people, one technician and one Ph.D., were making these monies, and I must say, we were pretty exploited because the whole company was over 30 people including janitors, and I was a

little naive. When I was hired the boss asked me, so how much do you think you are worth, and I said don't know, because I knew how much people were making years ago when I was there. I know that it was '81. Inflation in the meantime changed the buying value of a dollar, but I was making $25,000 a year in industry, making all these monies for the company, but I could survive, so I was happy because I wanted to survive in the beginning.

It went like this until I left Bachem. I was not really happy because once I learned how to do this, it was very monotonous work. There were 64 compounds which we were supposed to make, every day a different compound, but it was the same recipe, everything was done the same way. This was not what I used to do. I used to do every day something else.

KD: Did you think about going to universities? How did NIADDK come to your attention, become a prospect?

PK: Bachem made a mistake. They sent me for a meeting in Vancouver, Canada, to an international carbohydrate meeting to promote their products, which I did, and I maybe generated some business. But during that one week, I met my former boss from NIH, Dr. Glaudemans. I knew his work from before because he also was trained as a wood chemist first, in Canada, at McGill. Actually, I remember his major advisor, Dr. Timmel from McGill, came to visit our institute in Bratislava once. And because that was wood chemistry, I was assigned to go with him as a guide around the town, driving him to the

Institute. So I learned and I made acquaintance, and I knew his work with Glaudemans. So when I found out that Glaudemans was at the meeting, I tried to approach him and I did, and I had some friends from before who knew him. The editor at that time, of the journal where I was on the board, was also there.

KD: What was the name of the journal?

PK: The *Journal of Carbohydrates, Nucleotides, and Nucleosides,* which no longer exists. This is the journal. This is the first issue, Issue 1. You can see my name must be there somewhere.

KD: Here it is, the Slovak Academy of Science.

PK: It was in 1974. And that journal no longer exists.

KD: So you had some connections.

PK: Yes and that helped me.

KD: And you talked to Dr. Glaudemans?

PK: I talked to Dr. Glaudemans. He didn't promise anything. He said that he would explore possibilities because I was already established. I was not a beginning graduate who would

be suitable for a post-doctoral position. Two weeks later, I got a letter from him, that was in September, and in January I was already here as a visiting scientist first.

KD: What was Dr. Glaudemans working on?

PK: He was a very good immunochemist. He was studying immunoglobulins on a very theoretical basis. That was no translational research, that was basic research, and he in his study needed oligosaccharides. And he also knew my work in wood chemistry because he was a wood chemist. So it was a very good connection and he was very positive about hiring me but just didn't know how at that time, at the symposium. But then he offered me a position as a visiting scientist. That is how I started here working with him on this basic immunochemistry, but I was the person who didn't do the immunology work. I was synthesizing these very strange structures: flourosugars, dioxysugars, which he needed for mapping the subsites of combining area of immunoglobulins with antigens.

KD: He was doing vaccine work.

PK: No, he was not doing vaccine work. He was doing basic immunology, but not translational. We were very successful and I liked the work very much, and it was work which I could do. I was cranking out the sugars and he was amazed, and I was amazed because I didn't do flourosugars before. I didn't do the oxysugars before, but this was actually not so difficult. Once you study some literature you first just repeated the protocols that somebody else did and then as you do the work, you improve on things.

We published extensively and this also probably put me on the map around here. Glaudemans always emphasized, don't even think about getting a permanent position here. I accepted it, but I was doing still everything toward that goal. When he was thinking about retiring, which was about three years before he actually retired, I became permanent before that. I became permanent when I got my citizenship in 1986, which was five years after we came here. I was already considered for that. I was only waiting for my citizenship.

KD: All these publications didn't hurt.

PK: They helped tremendously.

KD: So you published more than usual, what kind of publications? How many papers are we talking about?

PK: I was writing ten papers a year because this was a new area where I could apply my ideas from before, new methodology. Also, I knew how to improvise, so I was making compounds which required something, which I didn't have to buy. I knew that the budget was tight and I surprised Glaudemans when I brought him something because he knew that I needed something for that and he never had to order it. So my improvisation ability, which again, the communist system taught me, was helpful. Some people came for advice and people came for compounds. I collaborated with some people at that time.

I was very productive, I must say, and this is what gave me the position because he knew that I can be useful. So when he was thinking about retiring, I knew that I will be here now probably taking over the section and I didn't know much about immunology. So I had to learn immunology. I was a chemist and I knew that I would not be able to survive with just making compounds, so I told Dr. Glaudemans that he should be engaging in something more practical. I wanted to change the line of work here so that it will help me survive here. I was interested in immunology because I found it interesting and during my making compounds for immunology, I was reading about all this and it somehow initiated my interested in these things. Dr. Glaudemans was a genius. I think he was a genius. He was so versatile. He knew so many things even outside of chemistry and immunology. He was a great violin player. He was a great painter. He painted like, if I didn't know that this was his painting, I would think it was some professional painter. He was very talented and he was a very good scientist. But through his violin playing he knew another scientist in another institute in Building 6, Dr. Schneerson, who was also a violin player and they played in some orchestra together. She was an immunologist, and they were working on vaccines, so this is how Dr. Glaudemans first established this collaboration with Building 6.

I also started working more on real vaccines, making not only oligosaccharides, but for antigens to imitate antigens which were involved in real diseases. This is how we first started working on Shigella Dysentery Type 1 and we published mapping, combining areas of immunoglobulins involved in that disease, and that was also very successful.

KD: This is the 1980s, early '90s?

PK: Yes, this was late '80s, early '90s.

KD: Was this the glycoconjugate?

PK: It was not glycoconjugate, but it was targeted towards that. We were still trying only to find out how the polysaccharides bind to the immunoglobulins to the homologous immunoglobulins, so we were making smaller and larger molecules as far as chemistry allowed because carbohydrate chemistry still has limited possibilities, making defined and well characterized larger oligosaccharides. There was another chemist involved in this because it was a very large load of work with shigella oligosaccharides and in Building 6, there was no chemical lab, so Dr. Schneerson, with Dr. Robbins, who was a lab chief, they hired a chemist who was working in our laboratory. He was officially employed with their institute, NICHD, Child Development. He was working here and then later they built a chemical laboratory for this person. And he moved to Building 6, and he took the shigella project with him.

I was in limbo, and I asked Dr. Robbins to think about another important disease where I could have my own project and he gave me some choices. Vibrio Cholera and cholera disease, I chose, because it was chemically challenging and interesting, and still useful for the medical field because it is a real disease, even though in the United States, here it is not really important, but thousands of people around the world die of the disease, even

though some vaccines are now commercially available but not really all that effective because they don't have very long protection. Cholera is still a problem and a good vaccine is still an issue that needs attention and that's why we still work on it.

KD: You talked about how Vibrio Cholera itself is complicated and a challenge.

PK: It was a challenge because the chemistry is complicated. Even though the structure is only a repeating unit of a monosaccharide, the monosaccharide is 12 chemistry steps to make from the commercially available material. It is a very complicated monosaccharide. It's a complicated structure, so making the monosaccharide is not so easy.

KD: Did you have to come up with the 12 steps? Was that your challenge?

KD: Not the whole 12 steps because that monosaccharide was synthesized before, but in a very cumbersome way and we improved on it. Then we started making oligosaccharides. Only disaccharides were known at that time. And we made 12 together, dodecasaccharides together, but it was good work. Later, circumstances somehow made it that we were no collaborating with Building 6, but Dartmouth Medical School had a physician who was interested in cholera and he actually found us.

KD: Who was that?

PK: Dr. Wade. He was a very good vaccine person and he discovered through the literature that we made this first, and with him, we made glycoconjugates first. And they tested it and they first found that the hexasaccharide when conjugated to proteins confer protection in mice.

KD: What is the layman's definition of the glycoconjugate?

PK: Glycoconjugate is any substance where a sugar is attached with chemically, not necessarily a vaccine. Anything, it's a general term. When we make vaccines, we actually don't make glycoconjugates, we make neoglycoconjugates. Glycoconjugates are usually natural products, but when man is involved it's manmade. (Should I say person-made?) Then it becomes neoglycoconjugates and these neoglycoconjugates can be made from synthetic carbohydrates or from bacteria. Polysaccharides happen to be on the surface of granulated bacteria and they are part of glycopolysaccharides, and when used as vaccines they can confer protection.

There are some neoglyconconjugates vaccines already available on the market and they are sometimes very expensive because they are usually made by first isolating these polysaccharides from bacteria. They have to be purified and then in order to conjugate them—these are large molecules, and proteins to which they are also conjugated are also large molecules. And it is believed that these two large molecules cannot really react unless we do something to make them reactive and still stay far away from one another so that there's no steric hindrance which will prevent them to combine. So what is normally

done is that both the polysaccharide and the protein are further reacted and further modified by attachment of some linking molecules so that these long chains keep these big molecules apart and only the small chains react together. But this is very costly because when you make this derivatization and attachment to link to either of these components, you end up with a mixture of chemicals and you have to dissolve these pure compounds, which you then conjugate.

KD: So you want to synthesize this.

PK: You have to synthesize that and then you have to purify it. This is all labor intensive and costly. And this is how even today vaccines are made. That's one thing. The second, which is common in vaccine production, is that these neoglycoconjugates are very poorly characterized because they are conjugated in such a way that at the end the vaccine is a large cross-linked molecule, and because it is very large and cross-linked, it is difficult to characterize it. So they are purified, but they are characterized to a certain extent, but many times we don't really know exactly what the structure is. We are happy that it works as a vaccine, not that you don't care what the structure is, but we don't have means to really determine it.

Now during our work on these vaccines, we didn't want to really make these poorly characterized molecules because we are chemists and we like to know what we work with. There is a method which can make well-defined neoglycoconjugates from small molecules from the synthetic oligosaccharides, and this is what I was doing with Dr.

Wade. We were making these oligosaccharides and conjugating them and in a special way using a chemistry which is called squaric acid chemistry because this chemistry allows making non-cross-linked big molecules.

This method was invented in Germany in the early '90s and it was working, and I've been using them for making all sorts of glycoconjugates, all known glycoconjugates because the method was developed to actually conjugate two amines together. We were using it for making glycoconjugates because when we attached this linker to an oligosaccharide and when the linker we modified to contain an amino group—these other amino groups are in proteins. Proteins are full of amino groups. So we were able to then conjugate protein which has many amino groups, with carbohydrate which had only one amino group. So these molecules, when they react, they cannot cross-link. So these molecules then are star-shaped. There's a big protein molecule and then rays of carbohydrates with the linkers shooting out, so this becomes a glycoconjugate because sugars are there, but not cross-linked fully characterized, but we can really very exactly characterize what those molecules are.

As years went by we were making all sorts of glycoconjugates from these oligosaccharides, not only for cholera, also for anthrax and for some other diseases. Then I don't how I think the idea that maybe we should try this important squaric acid chemistry also for the bacterial oligosaccharides, but without linker. So it was just a wild idea and it worked

KD: Do you remember when the wild idea came to you?

KD: We could find it from where our first paper on this was published. I think it was maybe 2004 or '05, something like that. Actually no, it was later, 2009, I think. When the polysaccharides—squaric acid and oligosaccharides we were doing before, but with this polysaccharide it must have been later because the first person who synthesized that in my lab was Dr. Shu, and he came later, 2001 probably. This is a very successful method and when they found it, it not only works, but when already Harvard University, in the meantime, established collaboration with Dr. Ryan at the Harvard Medical School, they also confirmed everything first what we did with Dr. Wade. So that's very important that you reproduce your results and the independent lab can confirm what you did with somebody else, so that was proof of the usefulness of this method.

Later we also did these neoglycoconjugates from bacterial polysaccharide, which Harvard University prepared for us. We are not equipped to work with infectious material, because you need to cultivate first and grow bacteria in a large amount, and then kill them and extract, and whatever. We are a chemical lab, so we don't do that, but they were able to do it for us and they gave us the polysaccharides, which is no longer infectious. We further purified it and then made glycoconjugates from it.

When it became known that this is going to work then I tried to patent this with NIH. I must say to my disappointment, NIH was not interested and they told me do whatever you want. They gave me permission to file or patent with the right person. I didn't do

that. I told Harvard University about this, who were ecstatic and they immediately jumped in. That's how we have a patent, with NIH's participation, except that the first patent holders are them, and this is how this successful collaboration is going on still.

KD: Are you to the trials stage?

KD: This is all a matter of money, of course. The government spent $2 million and hired an outside contractor, a biotechnology company, Paragon, in Baltimore somewhere, who ran this making of the vaccine, including growing this bacteria on a large scale. They took that protocol from Harvard and the conjugation protocol from us and they proved not only the reproducibility of our protocol, but scalability because this is what is important. As I learned in Bachem, it doesn't take only a bigger pot in order for something to work on a large scale. So they had to go through some explorations, but they were able to scale up and made a big batch. Because of shortage of money, it never went further to prepare a batch on GNP conditions so that it can be used then also for some clinical trials, first for toxicology and then through the whole process how a vaccine is approved eventually by the FDA. But all the basics are here, so it's really only a matter of money.

KD: Is this the cholera vaccine?

PK: This is the cholera vaccine. But in the meantime we don't do much more exploratory, some, but not much more exploratory work on cholera. We are now going into salmonella and shigella.

KD: Back to shigella.

PK: That is a different strain. Before that we also were working on anthrax because when anthrax became potentially a biological weapon, it was again, a chance situation how we got into that. It so happened that an immunologist from California came to NIH to meet somebody who knew his former advisor, late Dr. Kabat. Dr. Kabat was a very prominent immunologist who I knew through Dr. Glaudemans, and we also published together. When Dr. Wang from California came to look for somebody who might have known Dr. Kabat, he came to me because he knew that I was in the immunology lab and that we published with Kabat. So he came to visit and we had lunch together, and we talked about the weather and other things. At that point he said that he was looking for some collaborators who could synthesize for him the anthrax spore antigen, anthrax carbohydrate which is on the surface of anthrax spores. I didn't know anything about anthrax spores, but when he showed me the structure I thought that we can synthesize it, actually, and so we did.

We were the first people who synthesized a novel sugar anthrose which is the terminal determinant of a monosaccharide, which is on anthrax spores. We also made conjugates and we made with Dr. Wang and with some other important people around the world, some important diagnostic tools to detect the presence of anthrax spores. We never really got into making a vaccine because in order to work with live spores you need special laboratories and special equipment, and our hands were full enough. We were proud that

we made anthrose for the first time. Everybody wants to be number one in something, so I have ANTHROSE on my license plate.

KD: You've been talking a lot about some of the partners you worked with: Dartmouth and Harvard. You worked with external partners on anthrax.

PK: Yes, that was in Germany there was an institute of immunology, Robert Koch Institute in Germany, and they were able to make, using our sugars, monoclonal antibodies for anthrax spores with some compounds on anthrax spores, some proteins on anthrax spores. There was a publication from it and they were happy.

PV: How does the process work? Do you give them your paper, talk to them and say here you go, have at it?

KD: They usually find it. This is how first Dr. Wade found us. Through Dr. Wade I became friends with Dr. Ryan and these people in Germany and some other people in Australia, Japan and around the world, they usually find papers which are related in one way or another with their own work. If they feel that our chemistry can help or maybe we already have a compound ready for them because we have synthesized them, I make sure that every compound that we synthesize is still—that we have it in small amounts in a standard compound or sometimes a larger amount, and sometimes we send them. This is simply ethics in the field that if a colleague needs something then we send them it and we don't ask for anything. Besides, this was made with public money, so we cannot sell it,

but they usually appreciate it and then we collaborate and we participate in papers they publish. So this is a common thing.

Now days, science has become so complicated that unlike maybe 50 years ago you hardly ever see a paper with the same author. It's always at least five, six, even 20 or 30 authors because this is all a multi-disciplinary approach. Some people are like encyclopedias, but they still cannot go and work on a project from the beginning to the end and then come to some conclusions themselves. They have to have people from many different branches of science collaborating.

KD: Let's switch tracks. Dr. Glaudemans has told you don't expect to stay here, at one point, but then when he decides to retire, you stepped in behind him.

PK: I really don't know how it happened.

KD: Did he train you and get you up to speed on how the lab worked?

PK: No. I had been with him five years before that, so I kept my eyes open. Everybody has his own method. I adopted some of his ideas, how to be a mentor to some young people and how to keep the section going. This is a small group. It has always been a small group during my time. I remember that the group used to be much larger during previous management. I don't know how it happened that it shrunk almost every year, but when I started we were four people, three post-doctoral fellows and myself. Because it is a small

group and I tend to be in close contact, I talk to them every day, to every one of them, so the group was small enough for me to be able to keep track of everything: whoever works on what and at what stage. I still, even though I sometimes forget what I had for dinner last night, I remember still everything what is going on in the lab.

KD: How about the section? Do you have to go to the higher ups on a regular basis?

PK: Not really, not much, fortunately. I don't have many administrative duties. But I have a lot of editorial duties because over the years I became a frequent peer reviewer of scientific papers in my field. I am also on the editorial board of some journals and I have started my own series of books on synthetic carbohydrate chemistry. Volume number five is now in production, four volumes are already out, and it is very successful. I like doing it and it keeps me freshly informed about new developments, which helps also.

KD: That sounds like it would be big job. You must be talking to a lot of people, a lot of authors.

PK: I was involved as a sole person in volume number one because I didn't know how much work it was. But then when I discovered how much work it was then I always have a volume editor or volume editors. I am the managing editor, so everything has to go through me. But I am not involved in the recruiting of contributors. They have to write the letters, they have to initially evaluate whether any contribution is suitable or not. And only then it gets to my hands when I have to read it and decide how much it has to be

pruned because people usually don't realize that these chapters in the book are meant to be a dry protocol of making something. Then there's always some background introduction, but it's usually not more than a half page. I usually have to mark paragraphs which have to be taken out because it is not the purpose to give a review of something, it's only to give some reliable, reproducible protocol with properly characterized compounds where the preparations are described. So it's not like a normal publication for authors for which it is important that it comes out very quickly because the preparation of a volume takes three years. So if somebody wants to publish something quickly because it's almost a discovery then they don't send it to us, they send it to some other journal.

Yes, it is a lot of work. Because every volume, every next volume is more difficult to put together than the previous volume because usually important things which are generally useful have already been published and only a limited number of generally useful things are new. So it took me maybe one and a half years to put through the production from the beginning to publication of volume one. I remember volume four took almost three years to publish.

KD: It's probably getting more specialized as you go along.

PK: Not really because we want to cover compounds which are useful in glycosciences in many different branches of carbohydrates chemistry. When glycobiology comes into this, then more different compounds, different and modified carbohydrates are needed. But still, the first volume was more easy to fill with relevant material than volume five, which

is just about to be submitted, but still it's not out. I already have lined up volume editors for volume six, even though they haven't even started inviting people because I find that it would be not good if two volumes overlapped by inviting. So I'll wait until we close accepting papers for volume five and then I can give a green light to the editors of volume six to start their invitations.

KD: Talk about your open letter to the community of organic chemists, which makes for fun reading, and when you started developing those ideas, and the reception.

PK: The idea, writing something about the topic is a result of meeting colleagues in the field at various meetings during coffee breaks. We talk about many things and also where carbohydrate chemistry is going and what is the state of the field. And we almost unanimously agree that there is a crisis, not only in executing and publishing carbohydrate chemistry, but the whole field of organic chemistry, because it seems—well it is the truth because otherwise there would be not so much agreement that we have a crisis—that the more sophisticated instrumentation we have, and the more new useful chemicals we have to do our work, at the same time the science level of a huge number of papers goes down because everybody wants to do it quickly, everybody is struggling for funds. So if you don't publish quickly and don't publish a lot—publish or perish. Unfortunately, it has a negative effect on the quality of work.

People are worshipping “high impact factor” journals. I call these journals the “new golden calf” because not only are authors forced to do that because they know that the reviewers

are not looking at the content of the paper, but which journal is it, and in which journal people published before, and they judge competence and ability of young people by where they published before, which is not very wise. Young people cannot start publishing in some fancy journals even when they are talented and have good ideas. It happens then that young people struggle for funds, which are sucked up by established individuals who then, I don't want to generalize, get many times get funds to produce more sub-quality work.

We at NIH are fortunate that we don't have to write grants. On the other hand, resources are spent well because we are a bunch of self-motivated people who appreciate that we are allocated the funds and we don't have to spend time writing proposals, and we can fully devote our time and extra time to do research, and we do that.

When you come to NIH, Saturday or Sunday, 50 percent of parking lots are filled up and these are not filled up by bureaucrats. These are filled up by scientists. So there is no question whether we are motivated or whether we love our work or not. This is probably the best policeman that we are interested in doing things and also guarding things. We want to be number one and we don't want somebody to take advantage of us. So they don't have to be so nervous that we are going to disclose something which we should not, because we are interested in preserving the priority of our research. This is across the board, not only the old generation, the young generation also. We have many talented young people who also spend time here. I had a post-doc who actually came at midnight and it was not forced labor. She was interested in how things are going.

KD: Speaking of these younger scientists, you're handing things off to another generation. Where do you see carbohydrate chemistry going and the work that your lab is doing?

PK: Every field has it goals and it is good that carbohydrates are so heavily involved in the life sciences, so we have always tons of things to do. And there will always be need for a pair of good chemist's hands because our products are needed in such a wide spectrum of fields in the life sciences. It's not only vaccines. Carbohydrates are omnipresent in the life sciences. Even in the drug field, some useful drugs have carbohydrates as a constituent, so they are glycoconjugates, except not in vaccines, but for other things.

The field is going in the right direction except that, as I mentioned, many times we see that these materials which are synthesized are not always well characterized, well purified. Journals are accepting these works because somehow the publishing has taken over the science. Every day almost, a new journal is appearing because the publishing industry found that money can be made by selling journals. When the number of journals increases these pages have to be filled with something. When they have to be filled then the level of science has to be decreased, otherwise those pages would not be possible to fill. On the top of everything, with more papers there is a need for qualified reviewers and there are not enough qualified proofreaders, reviewers to read everything carefully. When I get a paper to review it takes me several days to do this. I have to go to the library. Even though my library is on my computer on my desk, I still have to go there to do it.

I was removed from the editorial board of one journal because I was rejecting too many papers. I found it a compliment actually. But that happens also because these publishers don't want you to reject the paper because they need something else to publish. This is not only chemistry. The life sciences in general, actually there was a paper published in *Nature* by the Director and the Deputy Director of NIH where they pointed to the fact that not everything is reproducible also in those fields and that it cannot go on like that forever, so we have to forget about high impact journals, and "H" journals.

I think that the metrics for the quality of science is not in H factors and impact factors, but the best factor is collected during meetings, during coffee breaks, how individual scientists are talking among themselves about certain scientists. Then you hear the truth whether they appreciate and respect some other scientist or whether they bad mouth them. That is the objective criteria, not the impact factor. Why would we put some value on the journal and not on the person who wrote the paper? Does anybody know where Einstein published his work? We value him and not the journal where he published things. I think it's a little bit misguided.

KD: You've had a chance to maintain a personal relationship with everybody in your lab.

PK: Oh yes.

KD: I get a sense that's how you mentor is just by working with people at the bench.

PK: Yes. I talk to them every day and I admit I don't do lab work per se. I sometimes do this or that, or show them something, but I don't have my personal project. I talk to them and we have also occasional journal clubs because always somebody comes up with something, so we discuss it. But we don't actually have regular lab meetings because I don't think it's necessary with such a small group when everybody knows what everybody is doing, and I talk to them every day. And I don't breathe down their necks. I give considerable freedom and this is what I learned from Dr. Glaudemans. He always said that putting pressure on people is a prescription for cheating, and I've never done that.

Two of the three post-docs come at ten, but they leave maybe at 8:00 at night, so why would I care when they come? Everybody has a different system how they work. I'm an early bird, but somebody else wants to stay long at home or do something and then comes later, I really don't make a big fuss about it. I know that they produce, I know that they do their job properly and that's what counts.

KD: Is all the work vaccine-related at this point and do you see it continuing in the future?

PK: That's a very touchy subject. I'm going to step on very dangerous ground, not because I'm two weeks before retirement, but, I retire, this section ceases to exist unfortunately, I'm afraid. I was hired with the intention of the Institute that the group should continue. I don't complain about NIDDK or the lab because on the lab level or the Institute level we have always been supported and I have no complaints about that. But I still think an

institution like NIH deserves a small group with the expertise in carbohydrates chemistry because they are important in the life sciences.

Our operation is inexpensive. Aside from salaries, our yearly budget is $70,000. With the billions of dollars which are invested in the NIH, this is a drop in the big bucket. And by dissolving this group, I cannot look at it in any different way than wasting of resources which have been invested in this group. So I don't want to keep it as nostalgia because this is a hundred years or more of the group, which is a nice history. And this is a history which contributed to the good name of NIH long before the DNA structure was cracked here.

I don't mean to be married to the past. Scientific counselors who evaluate us every four years, their reports have always been positive. I remember that one of the reports ended when they were talking about budget, that the resources of this group should be maintained or increased. In spite of that, 2019 came and this group is no longer going to exist.

KD: You can take solace in the work that you have done.

PK: Yes of course. All my wildest dreams as far as my professional life have been fulfilled here because, as I said, the Institute has supported our work. I have learned a lot in the process. I met fantastic people around NIH. At my age, it is full of brains and I am just a

little nut somewhere, but this is an excellent and very precious institution. This is a national treasure.

KD: And this has been a great story. I've really enjoyed talking to you.

PK: Thank you.