



VOICE EXPEDITION INTERVIEW TRANSCRIPT

The Oral History of Nephrology

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DWM: It's February 24, 2009 and it is my pleasure to be at the University of Missouri to talk to Dr. Twardowski about the history of nephrology. Dr. Twardowski has been a pioneer in dialysis therapies and is widely published in the nephrology literature about dialysis access, patient care and therapy parameters. He described the peritoneal equilibration test (PET) and invented the Missouri swan-neck catheter. He remains active as Professor Emeritus of Medicine at the University of Missouri. Dr. Twardowski I thank you for taking your time to let me come talk to you today.

ZT: You're welcome. Thank you for coming.

DWM: I need to start with where you were born and then where you were educated.

ZT: Well I was born in Poland in a very little village which is called _____ but it was before the second World War in 1934. I started education during the war. The war started in 1939 in Poland, that's how we consider the start of war. The start of war here is '41 but we had '39. We lived in the little village. My father was taken to a concentration camp because he was a doctor, educated, and Germans usually first took to the concentration camp the educated people. The reason was, probably, to subdue later the population if all educated people are gone. Anyway, so we lived with ... My father was a doctor and general practitioner. My mother actually decided that we should move from... Maybe I should start that during the start of the war we were living in _____, which was a part which later belonged to the Reich, Reichdeutsch, that means to Germany. As a matter of fact they didn't want us over there okay so they actually told us, you know, to go away. So because my mother had family in this village we lived with my aunt. In this place I started education from the first grade and so on. There were only four grades in this village and for the fifth and sixth grade I needed to go to the other village which was a little bit bigger and it was far away from this village but it was that much, it was about maybe, two and a half miles to walk. Right now children do not walk at all. But it was very good for me I think. Then for the seventh grade I had to go to the bigger city; it was already after the war and it was about five miles to walk but it was also very good for me. Anyway, my father ultimately came back from the concentration camp, he survived. He was moving from one to the other concentration...it's a long story but ultimately he was liberated by the American Army. He was ultimately in _____. He came back after. He was sick but he recovered and after about a year he came back to join us. Then we moved to _____ again because after the war, you know, this part belonged to Poland. I actually was going over there to school then for some time I was going to musical school but I was not very talented in music. My mother thought that I was talented but I was not. So ultimately I was educated in just regular, you know, high school. Then I moved to Krakow to medical academy, which was medical academy in Krakow. As a matter of fact for centuries it was Collegium Medicum of the Jagiellonian University but after the war I don't understand exactly why the communist government decided that the medical school would not belong to Higher Education Ministry, only to the Ministry of Health and so it was

moved from the Jagiellonian University and was called Medical Academy. Anyway I finished this in 1959 and originally I didn't have a position so I worked at as volunteer in the...

DWM: So you had no job.

ZT: No, I had a job. I worked in the emergency department. In Poland, at that time and I think even up to now, doctors drive to homes for emergencies to help. So I was working on an ambulance but as volunteer in the Department of Medicine. At that time they acquired an artificial kidney and...

DWM: What year would that have been?

ZT: Yes _____ I was asked whether I would like to work on the artificial kidney and so because that was a position I said, of course.

DWM: Sure. Would that have been about 1960?

ZT: This was in 1961, as a matter of fact, and I was participating in the building of the station, the dialysis station. I was helping in ...

DWM: Like the room. Like getting the room ready?

ZT: Room, getting the room and how to set up, you know, the artificial kidney. We got the artificial kidney called Alwall.

DWM: Spell that.

ZT: Alwall.

DWM: Okay.

ZT: This is a very famous Swedish nephrologist, one of the pioneers of dialysis. He was working on dialysis from 1945 so it was almost in parallel with Kolff.

DWM: Dr. Kolff. What did this Alwall machine look like?

ZT: Oh my gosh. I may show you. It was huge. If you want me to I can show you.

DWM: We've also got to describe it for me since we're recording.

ZT: This machine was a big tank and in this big tank were two cylinders, an inner cylinder and outer cylinder. On the inner cylinder the cellophane tubing was wrapped around and the outer cylinder was put to restrict the distention of the tubing during dialysis because if the tubing would be distended then the capacity of this dialyzer would be huge and the patient would bleed. So this was Alwall's invention as a matter of fact because in the Kolff kidney there was no restriction of the volume. The volume was restricted in some other way. I don't want to go into these technical details but anyway this restriction of the volume was the invention of Alwall as a matter of fact. Also it was possible, with this kind of

machine, to do so-called hydrostatic ultrafiltration that means removal of salt and water. In Kolff's machine ultrafiltration was achieved by putting glucose to the dialysate, okay, and was osmotic ultrafiltration. In this Alwall machine it was...

DWM: Pressure.

ZT: Pressure. Hydrostatic related. So this machine needed to be assembled before, of course, dialysis and one of my duties was to assemble this machine before dialysis. The dialysate to the small tank where these two cylinders were, the dialysate was coming with a huge tank which was in the other room and this dialysate was prepared before dialysis and it was usually enough solution for the whole dialysis; for six or seven hours of dialysis. My first experience with this Alwall dialyzer was not very nice because this was completely new and the first time when our boss decided suddenly, Dr. _____, decided that we would start dialysis because we had a case, okay. The building of this room was not yet completely finished also we didn't check this machine, you know, in any way. The decision was to just start it.

DWM: You have a patient...you

ZT: We have a patient and the patient would die so you know it's necessary to start. The problem was that it was... Maybe I will show you if I can how we _____ no I don't think that I have this. Anyway the first...always this inner cylinder was taken and the cellophane tubing was wrapped around and then the outer cylinder was pulled and then of course we needed to make some connection with the latex tubing, you know, attached to the cellophane tubing. Then the first thing was to find out whether this is tight, you know, everything. Whether there is some leak or not. So it was necessary to increase pressure inside and see what's happening. After I was doing this I put, you know, both things into water and pumped some air into it and I was very dismayed that the bubbles were coming, you know. What happened actually this...I don't know how you call this. There were some kind of sharp places, you know, so I had to take...as a matter of fact I took a file and I was looking where this is and I found it and put another one. It took me something like about 12 hours to assemble this. Then there was a problem because this Alwall machine was sterilized with boiling water so the dialyzer when it was assembled and I put it in water then I put the hose with steam which was suppose to go. What happened is the pressure of the steam was not enough to boil this water so I was very upset and I went downstairs or to the ground level where all these machines were heating water and making the steam. I was angry with the guy why, you know, this pressure is not high. He increased the pressure but it was still not going. Ultimately what happened when they were building all this they didn't actually close, you know, one of the holes in the wall and I was coming from down to the room and I saw that steam was coming from the other room where it was radiology. Ultimately it was fixed and it took another few hours and I was ready with everything the next day. The next day we did dialysis in this patient. As a matter of fact, you know, to make a long story short this patient survived ultimately. He had acute glomerulonephritis but he was young and 19 years old and ultimately he survived. We did a few dialyses on him and he was anuric but then he started to urinate and survived. One thing during this time is I suffered some kind of disappointment because I told you that this outer cylinder was restricting the expansion of the tubing but it was not completely. If there was some kind of increase in pressure then the volume was increasing. What I was calling potential capacity of the dialyzer was huge. So at some point the patient...we were of course filling the dialyzer with blood from the blood bank but then during dialysis the patient had hypotension because a lot of blood was going into this dialyzer when the pressure was

increased. It was really very difficult to deal with this. Ultimately we were able to save this guy but I was very disappointed with this machine; that it has huge differences in the volume. I was thinking about what to do about it. You know I thought that it would be necessary to invent a machine which would have a small capacity, small volume, but sufficient surface area for dialysis, for the diffusion or for dialysis. In this case diffusion through the membrane is called dialysis. So I was thinking really for a long time and I thought about different kinds of things and looking in the literature because I thought maybe somebody actually is making a better dialyzer. I found, you know, there was at that time Skeggs Leonards...

DWM: Skeggs Leonards. Yeah.

ZT: Skeggs Leonards and McNeil and these kind of... I looked also at some other machines but all of them were not very appealing to me. The construction was not very appealing to me. I remember that it was November 11th at 11:00 in the evening, I was falling asleep and suddenly I woke up and I started to think that capillary artificial kidney would be the best. I just jumped out and started to calculate what kind of capacity it would be and what kind of surface area and so on. As a matter of fact I calculated everything during this night and I decided to have this as my thesis for doctor of medicine because in Poland when you finish medical school you are called _____. _____ that means physician, but not doctor. Doctor here is M.D. and in Poland if you want to be a doctor you have to write a thesis. It would be like Ph.D. here.

DWM: Right.

ZT: But in Poland it was... As a matter of fact a similar something I think is in other European countries is the same system. But anyway ultimately I calculated everything and came to the conclusion that the best kidney machine would be... I will show you. This was ultimately published in 1964 but the idea came to my mind in 1962, as I told you, on the 11th of November in 1962. I was working on this, of course, and to write a thesis you have to go, you know, what was already available in the world and also it required, you know, some, I would say, theoretic background. Why, because I didn't make this kidney. It was not possible. In Poland at that time it was not possible to make this kidney because there were no capillaries to use them for this. I thought about making these capillaries and I tried to make them but I decided first of all, the theory is good, whether really capillary artificial kidney would be the best. So I wrote this thesis and I asked for this... This is my application for the _____. So I sent it in 1963, on April 9th 1963, I applied to open this procedure of getting, you know, the thesis.

DWM: A thesis.

ZT: Thesis.

DWM: Would you also have used this as sort of a patent to say this is my idea?

ZT: Yes. Yeah. At the same time of course... Before I published this I knew at that time I was talking with some people, you know how it is with patents and they told me before you publish anything you have to first submit a patent. So I submitted a patent and the patent was submitted on January 11, 1964. It was a Polish patent but the owner of this was the Ministry of Health. I was not the owner of the patent.

DWM: Ah, yeah. Yeah.

ZT: This is a little bit different, you know.

DWM: Right.

ZT: Anyway ultimately people decided that it makes sense, you know; the thesis is good and so I was awarded, you know, the title of Doctor of Medicine. _____ in the Polish language. Of course, I tried actually to do it in Poland because, of course, you know having a patent is one thing but doing this, it was very important for me. I was trying to convince the cellophane factory to make these capillaries and then they started to work on this but it was not easy. It was not easy extruding cellophane; it was as sheets was easier or as big tubing like, you know...

DWM: The Kolff drum used a big tubing.

ZT: Yeah.

DWM: Yes.

ZT: Like, you know, for this artificial intestine for sausages.

DWM: Yes. Sausages. Yes.

ZT: That's how it was. Then I found a guy in _____, which is one of the large cities and before the war it was called Breslau, it was in Germany but after the war it was _____. He was working over there and he was working with acetyl cellulose.

DWM: Yes.

ZT: And acetyl cellulose was easier to extrude and eventually later to saponify and make cellophane. As a matter of fact it was later done in this way. I started to work with him and he died, you know, and I just lost a partner to work with this. Nobody else was doing this kind of thing in Poland. I was thinking also about using natural fibers like from some herbs and one of these I found that it was a plant, which was called _____. Here it is _____. It is a tropical Asian perennial herb and they have a flex-like fiber from the stem of this plant and used in making fabrics and _____ and other things. They are long, you know, for instance _____ is very short.

DWM: Yes.

ZT: They are like, maybe, one or two centimeters. But these are about 8 to 12 centimeters. However the problem was how to make the bundle of that. Ultimately, you know, after a few years I quit because at that time I learned that Cordis Dow was...

DWM: Working on _____

ZT: Working on this and they made this kidney.

DWM: Yes.

ZT: In 1967.

DWM: Ben Lipps and Frank Gotch.

ZT: Yeah. As a matter of fact the guy who really started this was...his name, from Cordis Dow, was _____.

DWM: Hmm.

ZT: This was... _____ actually and I have his paper here. He, as a matter of fact, they started...maybe you know this story. That Cordis Dow worked on this acetyl cellulose and they were making these fibers for reverse osmosis to clean water.

DWM: Oh.

ZT: And Mahon came with this idea that maybe it would be good for an artificial kidney and he approached Steward and then Richard Stewart started working on this.

DWM: I see.

ZT: So this idea really was of _____; not of _____. But anyway Stewart was doing _____. I think that I have this paper here. He was coauthor of the first paper, The Capillary Kidney, and it was published in 1964 in the University of Michigan Medical Center Journal.

DWM: Hmm.

ZT: So the idea of this capillary artificial kidney, as many times happens in technology, it came to mind just not in one place but in some other places as well.

DWM: Right.

ZT: I tried, as a matter of fact, my patent was in January 1964 which was prior to any other patent on capillary kidney and I tried to secure a patent abroad but the owner of the patent was the Ministry of Health and before they would actually spend money on the patent abroad they needed to have the opinion of many people. Many people said, _____ especially, you know, these old professors they say, _____ will never work. One would say, oh artificial kidney would not be used; people would do peritoneal dialysis so it is absolutely worthless. Ultimately I got a good opinion of some other reviewers but the Ministry of Health summoned a special commission to patent the invention abroad and they did it on January 12, 1965, one day after the deadline.

DWM: Ah.

ZT: I was reminding them for about half a year; you have to rush otherwise it will be too late. This was one day after and of course this patent was not secured abroad, you know.

DWM: Yeah.

ZT: But anyway for me it was a very, very useful, I would say, experience with this. I knew how to deal with patents.

DWM: Right. Having gone through that process.

ZT: _____ Yeah. Yeah.

DWM: In those couple of years where you're thinking about the hollow fiber kidney and all that, I presume you were still taking care of patients.

ZT: Yeah.

DWM: Yeah. So did you all continue to use the Alwall kidney and was it successful?

ZT: Yeah.

DWM: And these were all acute renal failures, I assume.

ZT: Yes it was acute renal failure. But then I moved to another city in Poland. I moved from Krakow to Bytom. The story is also, I would say, interesting because there was some kind of accident in a coalmine. You know, the crush syndrome.

DWM: Yes.

ZT: You know, you've heard about crush syndrome. Crush syndrome was discovered or it was described by _____ during the war because after bombing London and people were crushed and, you know, there was crush syndrome. The artificial kidney was useful for crush syndrome. The Ministry of Coal Mine was upset about mortality. In Poland coalmines were very important because this was the only article, which was exportable at that time really. So they were putting a lot of effort, you know, to keep the coalmines working. They were unhappy about how the cases were dealt with. As a matter of fact they were thinking about sending to other cities but it was long distance. They were thinking about sending to Krakow or to Prague, to the Czech Republic. Ultimately they decided to build a hospital, a hospital for miners, and there were many departments but one department was supposed to be with artificial kidney. They didn't have any specialists at that time in Poland. There were not nephrologists.

DWM: They weren't calling people nephrologists.

ZT: No. There was no nephrology at that time. There were not many doctors as a matter of fact who were familiar with the artificial kidney. And even if they were, like in Warsaw _____ and one was in _____ but they didn't want to move to Silesia because they were established in these cities. My boss, _____, for some reason he said that we would move from Krakow to Bytom because it would be good

to develop, the Ministry of Health has more money and eventually it would be possible to expand and so on and so on. There were also some other reasons ultimately. We were married but we didn't have an apartment. We lived with the parents of my wife and after moving to Bytom we received an apartment, you know, as a token of being employed over there. So this was one of the reasons why we moved. There were also some other reasons but anyway this was the most important. Ultimately _____ didn't come and I built really this kidney center or kidney laboratory or whatever kidney unit; artificial kidney unit. I was left alone. At that time I was very young, I was only 29 _____.

DWM: So in what year would that have been?

ZT: When I moved, it was in 1963 so I was doing my thesis in Krakow but I was already living in Bytom okay. You know that it takes time.

DWM: Um hmm.

ZT: So I applied for this thesis in April but I moved to Bytom in September. I started to work on this and ultimately in 1964 the kidney center was working. But we had different machines. This was a coil dialyzer and it was a _____ machine, which was pretty similar to the American Baxter machine.

DWM: Um hmm. So in 1964...

ZT: 1964.

DWM: You are an acute dialysis unit.

ZT: Unit.

DWM: How many patients were you dialyzing? How often were you getting the machine ready and dialyzing people?

ZT: As a matter of fact I had this crush syndrome patient I had some, and I even started to dialyze more frequently than it was used to being.

DWM: How often were you dialyzing?

ZT: I dialyzed daily this patient.

DWM: Why did you decide to do that?

ZT: One of the reasons was that these patients had very high catabolism. Also, there was a paper of Dr. Teschan

DWM: Paul Teschan.

ZT: Paul Teschan about prophylactic dialysis and I was very much convinced that this is the way to go. Not waiting on the patient would have, you know, the absolute indication to dialysis. Of course at that

time there was a little bit of fear that dialysis may cause some damage to the patient so, you know, it was not like today we have better equipment and nobody thinks about the dialysis may do some damage. But at that time it was a little bit different, you know, so frequently people were waiting until potassium was close to 7 otherwise they would not then it would be justified; people would justify it. We needed to do it otherwise the patient...

DWM: Was dying.

ZT: ...with high potassium would die. I remember even that somebody from the coalmine; when I was talking about that we have to follow some rules that potassium has to be 6.5 that means closing to 7 then we can start dialysis. He asked me, why do you need that, you know that actually in a few hours this patient will have, you know, _____. Why do you need to do that? To be honest, you know, it was eye opening. I said some people do more frequently; they will use prophylactic dialysis. I started really to do this prophylactic dialysis, I dialyzed these patients daily.

DWM: How did they do? How were your outcomes?

ZT: As a matter of fact, I published a paper in 1972 about my experience with prophylactic dialysis and we had low mortality with this crush syndrome. We had survival; 80% of patients survived, which was absolutely unusual but they didn't have infections. You know this is a little bit different story. It sounds, you know, incredible but it was true that mortality was low with this prophylactic dialysis. They were crushed but they... For instance, soldiers had wounds and other and it was different, you know, so Teschan had higher mortality but he had wounds, which were infected. We didn't have wounds. This was crush, the patient had crushed muscles but the skin, most of the time, was not open.

DWM: Right.

ZT: And so this was probably the difference. But anyway I was convinced about, you know, this frequent dialysis. To talk about some other things; I didn't have enough of these acute cases as a matter of fact and I started to think about doing some chronic dialysis, which I read about the chronic dialysis. In Poland at that time chronic dialysis was not done at all.

DWM: We're talking the mid 1960s to late 1960s.

ZT: It was 1967 when I started doing this chronic dialysis. It happened also by accident. There was a patient, she was a bricklayer I think, and she fell from the... How do you call it?

DWM: Like a scaffold?

ZT: A scaffold, yeah. She fell and she hit herself in this region and the kidney burst.

DWM: Yeah.

ZT: So she had ruptured the kidney and they, because she was bleeding profusely, they removed this kidney. They didn't look at the other and the other kidney was underdeveloped and it was inefficient. She came to me and I started to dialyze her and I saw that she didn't have any urine output, anything.

How come? She should have something. Then we started to think that probably this other kidney is worthless and as a matter of fact we found really this other kidney is worthless. But we started to dialyze and what to do with this patient. Ultimately I dialyzed her, I think, for a month or something and then I started to think about transplanting this kidney. There was no kidney transplant program in our unit so I sent her to _____ and they transplanted the kidney but this transplanted kidney didn't work as well. As a matter of fact this was the first transplant in Poland.

DWM: Wow.

ZT: I was coauthor, of course, of the paper on the first transplant in Poland.

DWM: Sure.

ZT: But it was an unsuccessful transplant. The first successful transplant in Poland was made in Warsaw and it was a few months later.

DWM: So she...

ZT: See then what happened is I started to think about, you know, doing ... I was not using this machine all the time so I was thinking, you know, why actually not using it for something. Then what happened is a young lady, the daughter of a very important person in Ministry of Coal Mines, suffered chronic kidney failure and of course nobody accepted her and the father came to me and said how he would be able to help me if I would take her for dialysis. So ultimately he put a lot of money to expand, you know, the unit so we rebuilt the unit. Also he bought four machines for us and so we had four machines.

DWM: Wow.

ZT: And we had RSP machines, this Baxter. The problem was with dialyzers. We had dialyzers but they were not very good dialyzers. Also for each dialysis we needed one dialyzer and ultimately this chronic dialysis program started and was going.

DWM: And this was the late 1960s?

ZT: For really chronic dialysis it was from 196____. I have to look at this.

DWM: That's fine.

ZT: Because I don't remember. The real chronic dialysis program started really something like '67 but I have to look at my... I don't remember exactly everything.

DWM: Well of course there was the issue not only of the machines and the space for chronic dialysis but access was a huge issue. What were you all doing about access?

ZT: I was using Scribner shunts.

DWM: Scribner shunts.

ZT: As a matter of fact I made them by myself.

DWM: Tell me about making a Scribner shunt. What was that like? What did it take to_____.

ZT: I bought Teflon. Teflon was not available in Poland. Originally I used polyethylene shunts, which were made in Poland, but these shunts were not working for a long time because polyethylene was irritating and also clotting was pretty quick and so this was not working. So I was doing in some of the... For instance in this patient, this daughter, I was doing cannulation of the femoral artery and femoral vein.

DWM: For every treatment?

ZT: Originally for every treatment but later I was leaving this in and making, you know, the connection, a silicone rubber connection, between the artery and the vein. But of course this was only for a while and then I was using Teflon. I remember I bought a hundred feet of Teflon and I was able to extrude the Teflon to make a little bit smaller because the size of this was, I think, 2.5mm or something like that so it was necessary to pull it.

DWM: Heat it over a flame and pull it.

ZT: Heat it over and pull it.

DWM: Were you getting it from the United States from Dow?

ZT: I was getting it from Seattle.

DWM: _____ Like Scribner was helping you get the Teflon tubing.

ZT: No actually I don't know how ... it was not going through the Ministry of Health only through the Ministry of Coal Mines and they were buying it for me. They were buying the Teflon for me and also they bought silicone rubber for me. So it was relatively easy, ultimately, to make a connection between Teflon into artery, Teflon into vein and connection with silicone rubber. Originally I was using this method of Quinton with heating and making, you know, bending this Teflon but it was very, I would say, very difficult to do it. Once I got silicone rubber it was so easy to make a connection between the artery and vein. So for some time I was using...ultimately I got the original Teflon silicone shunts from Quinton Company.

DWM: They would send you the whole shunt?

ZT: Yeah.

DWM: Did you learn about these shunts and how to put them in just by reading about them?

ZT: Reading.

DWM: In the literature? You weren't traveling to see ...

ZT: No I didn't see it anywhere.

DWM: You would just read about it?

ZT: I read about it and I put, you know, this cannula. I was doing... Our surgeons were not doing these. Actually I didn't have a surgeon to help me.

DWM: You just taught yourself how do it?

ZT: So I learned how to do it and I was doing this. At that time many nephrologists were doing this kind of thing, you know. I didn't think about it. We didn't have vascular surgeons and so it was, as a matter of fact, not difficult to do it. Just cut it and do it. I had pretty good survival. Some of the shunts survived more than a year and I was pretty happy until maybe in 1969 I decided to use arteriovenous fistulas. Also I was doing it by myself, this fistula.

DWM: Just taught yourself how to do it?

ZT: Yeah, how to do it and I read, you know, the paper of Cimino and Brescia.

DWM: Brescia.

ZT: Brescia and Cimino _____. As a matter of fact I was doing side-to-side anastomosis as it was done originally by Cimino and _____ was the surgeon who was doing these. I was making some progress as a matter of fact I made some innovations, I would say, on how to do it. For instance, this is not done right now even. I was always tying off, you know, collaterals. It depends what collaterals. I have pretty good veins.

DWM: Yeah. Yeah.

ZT: I love this kind of vein. When I look at this vein I would put a fistula in it. But here you see that the vein is going like this but here is the collateral one and the second.

DWM: Right.

ZT: Usually I was tying off these collaterals just to have only one stream of blood going because it was better, you know, just to cannulate and get enough blood coming. These collaterals...if somebody is doing it and not tying off these collaterals the blood is going everywhere and it's not going through the fistula where it should. Anyway so these fistulas, I started I think in 1969, these fistulas. So it was three years after this paper by Brescia and Cimino and _____ and _____.

DWM: How was your chronic program? How many patients were you dialyzing?

ZT: Ultimately we dialyzed day and night. I had ultimately 14 patients.

DWM: 14 patients in the late 19 ____

ZT: On four machines, yeah.

DWM: That was a huge program.

ZT: Huge. It was a big program. It was, as a matter of fact. I mentioned to you that I was kind of enchanted with the idea of frequent dialysis, prophylactic dialysis, and I started to do some study on the adequacy of dialysis. This was my thesis for _____ doctor of medicine. There is nothing like that in the United States. But in Europe if you want to be _____, _____ is like just below professor, okay, _____. Here we have only assistant professor and associate professor but it would be something similar to an associate professor. If you want to be an associate professor, that means _____, in Poland at that time you needed to have a thesis _____ thesis. So it's like a second degree of thesis. The same is in Germany and I think in the Netherlands. It's not in England. I think in Austria it is the same. I don't know how it is right now because it is changing very rapidly. But at that time it was necessary. In the future I wanted to be a professor so I needed to have this thesis for _____. In Polish language it is _____ doctor. I was working on the adequacy of dialysis and I was comparing the different kind of laboratory tests to the clinical. I was convinced that the most important indication of adequate dialysis is clinical. How the patient is doing, what symptoms, what signs and so on and so on. Ultimately I found that with proper dialysis that the symptoms of uremia can be eliminated like, of course you know, insomnia and restless leg syndrome and many others. Symptoms which, even right now, people do not consider that these are symptoms of uremia because they are going by Kt/V instead of the clinical picture. Also I have to tell you that I was so convinced that more frequent dialysis is needed so I was going to more frequent dialysis and we, at the time, are doing twice weekly then I was doing three times weekly and then if there were stubborn symptoms I was going to four times weekly and in some patients six times weekly dialysis. This thesis I wrote the papers in 1974 and '75 and at that time I was convinced that daily dialysis would be the best one. As a matter of fact I concluded my paper, the last paper of the series, I concluded with the statement, I am convinced that in the near future daily dialysis will be the basic form of treatment of uremia. It was in 1975. In Poland, to be honest, I was not very eager to work _____. At that time I had in my mind a machine for daily dialysis but I didn't try in Poland to make this machine because I knew at that time it was impossible. Absolutely it was impossible. But then I came here in 1976, the first time.

DWM: To Missouri or to the United States?

ZT: To Missouri.

DWM: Was it your first trip to the United States?

ZT: The first trip to the United States was in 1976. I was invited by Dr. Nolph for a fellowship.

DWM: How did you meet Dr. Nolph? How did you _____.

ZT: As a matter of fact one of my friends, Dr. _____, he came here and he worked here with Dr. Nolph and he was liked by Dr. Nolph and he said if you have any colleague who would like to come I would be happy to have him. He said that I have a friend who would be very good for you and so Dr.

Nolph invited me and I came here. I worked as a fellow but also I was involved in some research at that time. Among other things I was working with Dr. Nolph on peritoneal dialysis. Dr. Nolph was mostly interested in peritoneal dialysis.

DWM: Had you had much peritoneal dialysis experience?

ZT: I had. I also wrote a paper on peritoneal dialysis when I was in Bytom. I had a lot of patients because, you can imagine, I have four machines and 14 patients and there was no way actually to put any more. So the only way to do it was to find out some other way and the only way was peritoneal dialysis. Only patients from peritoneal dialysis could ultimately go to hemodialysis. The peritoneal dialysis was like...

DWM: They started with PD and then could go.

ZT: Started PD and then could go. But anyway I had some observation on peritoneal dialysis. Also I was doing my own intraperitoneal catheters because actually the catheters were very expensive so I was using polyethylene tubing made making you know side holes and things like that.

DWM: You were making your own PD catheters?

ZT: Making, yeah, PD catheters, yeah.

DWM: And you were inserting them using the trocar and then...

ZT: I was inserting them with a trocar; yeah, I was using a trocar and other things.

DWM: How were they doing? How were those catheters doing _____?

ZT: They were doing not that well, to be honest.

DWM: What problems were you having?

ZT: There were leaks around, leaks and infections and others. But ultimately also I didn't have good peritoneal dialysis solution and there were problems with pain, intra-abdominal pain after infusion of this fluid. It was...

DWM: And were you doing... Would they come into the dialysis unit and you would do exchanges for some period of time and then they would go home?

ZT: No, they were coming. You know they were coming to the center like twice or three times weekly.

DWM: And you would do several exchanges over some period of time.

ZT: Yeah. I was doing multiple exchanges.

DWM: Then they would go home for a couple of days without dialysis and then they'd come back.

ZT: Yeah.

DWM: So an intermittent peritoneal...

ZT: Intermittent peritoneal dialysis. As a matter of fact I had an idea about doing something different like more frequent exchanges done at home. As a matter of fact I was invited, in 1974, to Italy by _____ Company. At that time I had some connections with reps from different companies. They came to me because they knew that I was doing something in this Bytom. So they were coming and they invited me to _____ Italy, to _____ Company, and I presented to them the idea of doing dialysis exchanges several times per day. As a matter of fact they didn't buy this idea and I later talked with them and they didn't want this idea. Then Moncrief and Popovich did it in 1976 and he told me, if I knew at that time that it would work _____ it was too late _____ you have to try it then you can find out whether it's possible or not. I was talking about these bags and others but at that time it was not a proper time to do that. But anyway when I came here to Columbia, Missouri I was working on... My gosh, it's getting late.

DWM: We've got a little while longer, yes.

ZT: Yeah. So I was working on some peritoneal dialysis and I was involved in this continuous ambulatory peritoneal dialysis that one of the first...

DWM: That Austin and Columbia jointly worked on together.

ZT: Jointly worked together, yes. Also I was working on... I noted something in Poland that one of the patients who had psoriasis and was on dialysis; the psoriasis disappeared. I had two such patients. I wrote a letter to the Annals of Internal Medicine about this kind of observation. Then we were doing some studies here on psoriasis. As a matter of fact psoriasis is helped by dialysis but the treatment is, I would say, worse than the disease.

DWM: Nobody wants to go on dialysis to cure their psoriasis.

ZT: But there are patients with severe psoriasis, which would benefit from it. It was for sometime people were doing this dialysis for psoriasis but it's not accepted right now. There are better medications right now and so nobody does it. But anyway we were working on this at that time. I came back to Poland because I was suppose to be here only one year so in 1977.... And also there was another thing. They needed a Chairman of the Department of Nephrology in _____. It was not easy to go abroad because as maybe you know the communists do not like to let people go abroad. I am saying frequently that this is like in feudal time you know about the peasants who _____ that means they were assigned to the lot and they were not able to move. The communists consider citizens as their property and so citizens should not go abroad. I was allowed to go abroad under the condition that my wife and my children would stay in Poland. This was one condition. The other also was I promised that when I came back I would go to Lublin and be Chairman of the Department of Medicine. I already had this _____ and everything that was needed and that I would actually continue to develop this Department of Nephrology in _____. So Dr. Nolph, as a matter of fact, mentioned that he wanted me to stay but I promised to be back and I didn't want to break my word which I gave to somebody in the

Ministry of Health. Also my wife was not very eager to come to the United States. At that time, even if I stayed, my wife probably would stay in Poland and we would be separated so I came back to Poland. But then the situation changed in Poland. The solidarity movement, it looked like communism is gone and it was possible to travel so I came again. I met Dr. Nolph, I think it was, in Amsterdam we met and I started to talk about some idea about looking for a new osmotic solution substance for peritoneal dialysis. Dr. Nolph said, okay just come over and work on this. So I came here and I was working. As a matter of fact from this study nothing came out. I was working on gelatin as an osmotic agent and we did some studies in rats and this gelatin was absorbing such huge amounts that it was impossible to use gelatin. As a matter of fact this actually led us and Dr. Khanna was very much interested in why so much of this gelatin is absorbed so it is going through lymphatics and there were studies on lymphatics in peritoneal dialysis and Dr. Khanna was mostly interested in this problem. But anyway then martial law was imposed in Poland and Dr. Nolph, as a matter of fact, lost I think one or two faculty and he really wanted me to stay. When marital law was imposed the plan was to bring my wife in January and try to convince her that she would come. We were supposed to go to New Orleans for some meeting and also to show my wife, you know, how nice it is here. Ultimately it was impossible because the martial law was imposed and I couldn't communicate. Originally there was no communication but then I was able to communicate and I sent a message that I would like them to come, if possible, because I thought that communism would stay in Poland for a long time and I was intolerant to socialism; communism for me was so obnoxious that I wanted absolutely to go to the free country. Also at that time, as you know, here was Reagan and the country looked so great. Ultimately we communicated with my wife. My wife was not eager to come but particularly my older son wanted to come and my younger son also agreed and a letter was written by my older son just to stay, don't come here and we will come sooner or later. For my wife it took four years to join me but ultimately she came in 1985. But she doesn't regret it right now. We can go right now to Poland to _____. We live in Poland for about five months a year right now.

DWM: Come back here, yes.

ZT: _____ come back here. But when I came here, to be honest, I thought about this machine for daily dialysis.

DWM: Yeah.

ZT: First of all, of course, I disclosed my invention to the University and then started to look for, first Baxter... we were very much... Dr. Nolph worked with Baxter. I was also working with Baxter on some other things like, for instance, these osmotic agents. We were working with Baxter and they were putting some money, we patented this ultimately and things like that. But, as you know, you have 20 patents but only some of them really are good enough and only a small proportion give something regarding the royalties. Most of the patents are worthless ultimately. You know you try but.... My saying is: I have three good ideas in my mind, if one is really good it's fine; so two are lost but one is good. Anyway Baxter originally started to work on this machine but ultimately decided not to and there were two reasons. They told me that first of all they would put in a lot of money and nobody knows whether it would work and the second is if it works then we would cannabilize our peritoneal dialysis program. But at that time peritoneal dialysis was going really, really fast up but then peritoneal dialysis started to go down. I went to them in 1988, I think, again trying to convince them that they should actually take this idea but ultimately they decided, no. But I was also working with Rod Kenley

ZT: You may hear about him in the future, you know. I was working with him on tidal peritoneal dialysis. Do you know tidal peritoneal dialysis?

DWM: Yes.

ZT: I was working with him and at some point we came to the conclusion that for the tidal peritoneal dialysis it would be good to have some kind of machine making the solution. Baxter decided against and this was a decision, I think, a financial decision. I don't know. They were afraid that people would take this machine and manufacture peritoneal dialysis solution or something. I don't know exactly what was the reason. But they scratched this program. Rod Kenley was even more upset about this than I. We met in San Antonio. There was an American Society of Nephrology Meeting in San Antonio and I talked with him for about 10 hours. I presented to him the idea of daily home hemodialysis and he bought it. He was working at Baxter at that time and he was trying through his channels to convince them but they were adamantly against it. Ultimately Kenley left Baxter and founded a company, Aksys.

DWM: Aksys.

ZT: And he told me actually that I should patent this _____. Of course I disclosed the invention to the University but the University was originally trying to find somebody but they didn't patent this and I told them that I would like to patent this. If they don't want to pay for the patent I would pay by myself. So they gave me a waiver from this invention, okay, and so I ultimately patented this and the patent was taken by this Aksys Company. This Aksys machine is based on my patents. As a matter of fact I have five patents for this machine.

DWM: Parts of the machine.

ZT: Part of the machine, yeah. And that's how it was.

DWM: Yeah, an amazing story. During this time that you came to Missouri and you had this vast dialysis experience in Poland, I mean running one of the early chronic dialysis programs, taking care of patients on peritoneal dialysis, waiting to have a hemodialysis time. When you came here did you spend most of your time working on research or did you still take care of patients?

ZT: I took care of patients. I had quite a bit of patients. I had some time for research but I was... wait a second, I had six months of clinical work plus I had my dialysis patients but most of my free time was for research.

DWM: Okay.

ZT: I didn't have too much free time.

DWM: No.

ZT: Usually I worked about 12 hours per day; that's what it is. Somebody wants to do something and needs to do...

DWM: Yeah.

ZT: It's impossible to do, you know, like 40 hours per week. No.

DWM: Oh yeah. No. Well because during all of this time that I've know about peritoneal dialysis in the last 25 years, I mean, you've been involved in some continued improvements. Well, the peritoneal equilibration test.

ZT: Yeah.

DWM: Which is really research oriented but I'm sure came from clinical experience also.

ZT: Yes. I will tell you about this peritoneal equilibration test.

DWM: Yes, yes, yes, tell me.

ZT: In most of these papers in the introduction somebody should say how it came about. But usually this introduction is not exactly as it was. When I was working in Poland... This is a fascinating story. When I was working in Poland one of the patients on peritoneal dialysis had nephrotic syndrome. Nephrotic syndrome is a lot of protein in urine then she lost completely urine output. Her kidneys didn't work but I started to think about does she have also higher protein losses on peritoneal dialysis. At that time I didn't know that these changes are only in capillaries of glomeruli. I thought maybe these changes are everywhere and so maybe this lady has a lot of protein. I didn't see anything different on her in peritoneal dialysis clinically but I decided to measure how much protein she has and how much protein other patients have in peritoneal dialysate. So I did some study and I found, first of all, that she had the lowest losses of protein where some others had different. I repeated these studies in the patients and I found that patients had their own protein losses. If they have, let's say, 20 grams per day per dialysis it is about 15 to 25 but around 20; if they have 10 they have 10. If they have 40 they have 40. So when I came here and started to think about... You know at that time I was disappointed about this gelatin, that it was not working and I was thinking what to do that the patient would be selected for best peritoneal dialysis for them. I recalled this, my observation, that maybe these patients have everything stable and different. That they are different. And that's what started, you know, this peritoneal equilibration test I decided to do in patients. This patient had this kind of curve, this curve _____. It took some time but we ultimately came to the conclusion that really patients have individual transport characteristics and then we divided them into high transporters, high average, low average, low transporters and so on and so on. But this was the beginning of this test. Prior to this everybody was measuring only mean values and standard deviation but then I came with this idea that probably the patients differ in peritoneal transport characteristics. It came from this observation about this protein and the protein was from a very false assumption that probably the patient has higher protein losses, you know, when she was nephrotic. At that time I didn't know that it was _____. I don't know whether it was known. I think at that time it was not known that is only in capillaries of glomeruli.

DWM: Right.

ZT: I think they discovered it later. I think.

DWM: Yeah. Well the peritoneal equilibration test and recognizing that different patients have their very own individual membrane characteristics has been a very big contribution to understanding peritoneal dialysis.

ZT: I think that many people are using this.

DWM: Yes.

ZT: I will tell you also another thing about... I mentioned to you about this lady, the daughter of this important person ...

DWM: Yes. _____

ZT: In the Ministry of Coal Mines. She was one of the patients whom I put in a fistula. For some reason it happened that she had very short segments of usable fistula and because of that my nurse who was excellent... She is deceased now. But she was excellent in puncturing fistulas. The fistulas punctured originally were punctured by me but then I got some kind of permission that nurses would be allowed to do this. But she was an artist, I would say. She was doing this sticking of the fistula and she was sticking in the same spot. The patient told me that she said that she noted this is not painful. Whether it is possible to stop, you know, using lidocaine. I said, why not. If you don't have any pain, why use lidocaine. So she was not using lidocaine. Other patients learned about this and asked me whether it would be possible to have the same method of sticking fistulas. I started to think maybe it's a good idea and so within six months every patient in the center had this method which we called constant site puncture method.

DWM: Which now we call?

ZT: Buttonhole.

DWM: Buttonhole.

ZT: Buttonhole method. By the way this patient had this method used for 26 years. After 26 years she lost the fistula, there was no possibility of doing another fistula because she had very, very arteriosclerotic arteries and one of the reasons was that she had myeloma multiplex. I think that this was related a little bit to dialysis, which we were doing on her with kind of dirty dialysate. You know that she was stimulated and she developed myeloma multiplex and arteriosclerosis ultimately. But she survived 33 years ultimately all together. The last seven years she was on intravenous catheters and dialyzed.

DWM: Um hmm.

ZT: I learned from the guy who followed me in Bytom.

DWM: Once you came here. Yeah. Yeah.

ZT: But anyway so this buttonhole method, you know, like many discoveries this was serendipitous. It was not my discovery, it was really... the only thing my, I would say, role in this was that I didn't dismiss it, you know, out of hand. Many doctors are taught by patients many things and doctors frequently just dismiss it. But I've found that patients have excellent observations.

DWM: They do and particularly dialysis patients.

ZT: Oh yeah.

DWM: They have this complicated treatment and they understand their bodies and their response to the treatment very well I think.

ZT: The last story I will tell you about called...you heard about daytime ambulatory peritoneal dialysis.

DWM: Um hmm.

ZT: This was invented by a patient here, my patient, Mr. _____. He came one time to me and he told me that he doesn't have ultrafiltration when he is overnight, having an exchange overnight. During the daytime he has some ultrafiltration. He asked me, why should I do overnight if I don't have any drainage and so I decided to do it only during the daytime and I am empty during the night and is that okay? I told him, this is wonderful. Why should you do it this way if this is not working? I started to write a paper and I called it the _____ Technique. Ultimately I didn't write this paper and the reason was that this patient, for some reason, committed suicide and so I was kind of uneasy about writing this paper. But this was really the patient's idea about this daytime ambulatory peritoneal dialysis. Right now we call it daytime ambulatory peritoneal dialysis but it is really the _____ Technique.

DWM: Just listening to this, I mean, how much of your work you have done has been observation and just thinking, thinking about what you're seeing every day. How important that is.

ZT: I think that this is extremely important but if somebody wants to do something innovative he has to observe and not reject some idea out of hand because it may be that this idea is good. This is different than, for instance, some confirmatory studies. You do prospective randomized type but already these ideas have to be that you can compare something to something.

DWM: Right.

ZT: But first I learned that Dr. Scribner, for instance, his idea about the shunt came overnight. He just woke up and he started to think that if I have actually the blood access in this patient I can keep this patient forever, you know alive forever. This came in the middle of the night, this idea.

DWM: Yeah.

ZT: He didn't reject it out of hand. He was also saying that he didn't do any animal studies and he was lucky that he didn't do it because in animals this arteriovenous shunt doesn't work in animals, only in _____

DWM: _____ Also I have talked to people from this time in the 1960s when innovation in dialysis was just happening pretty rapidly and they note that if they had had to deal with then all this regulation and approval and everything that we have to do now that a lot of things would not have happened.

ZT: Absolutely. Absolutely.

DWM: Yeah. I mean I think about what you were doing in Poland where, I mean there was a necessity, there was a need there and you taught yourself and you did it.

ZT: I did reuse of dialyzers. I introduced in Poland. I have a patent, you know, how to reuse dialyzers in Poland. And it was, why? Of course you can figure out why. I was using glucose-free dialysis solution and this was because... it's also a very interesting story why I wrote the paper about this; glucose in dialysate, why I was using it. The reason was that the glucose was very expensive, you know. It was the most expensive ingredient of dialysis solution.

DWM: Right.

ZT: But also reuse, of course I could reuse six times. There was a point when I had four machines and I was told that I would have only 1200 dialyzers per year and I was just kind of, you know, it was times less than I needed and this was the reason I started to work on this reuse of dialyzers. Ultimately I was able to reuse five times, six times was the maximum but it was five times exactly as needed.

DWM: Just right.

ZT: Just right. As needed.

DWM: It sounds like when you were in Poland, up until the time you came here and there was sort of more freedom to travel, you could not really have gone to many meetings or anything like that.

ZT: No.

DWM: Once you came here in the mid 70s or late 70s, did you participate in the... I know you've been ASN and I know you all had your annual dialysis meeting. Did you get involved in ASAIO at all?

ZT: In ASAIO a little bit, yes, originally. I presented something on ASAIO of course, two or three papers I presented on ASAIO and in ASN and some other but right now I only go to our dialysis conference.

DWM: Well it's very big and comprehensive, so yeah.

ZT: Also right now I'm more interested in the history of dialysis to be honest, you know.

DWM: Sure.

ZT: I'm writing some papers on the history of dialysis.

DWM: When you're writing those papers and thinking about the history of dialysis; who are the important people? I mean if you had to pick out just a handful of people and events that really are pivotal, what would you say?

ZT: In peritoneal dialysis just two people. Of course Frank, Seligman and Fine. These three people.

DWM: Frank, Seligman.

ZT: Frank, Seligman and Fine. _____

DWM: J. Fine.

ZT: J. Fine, yeah.

DWM: Okay. Why are they so important?

ZT: They did actually the first dialysis in humans, which saved the life of the patient.

DWM: Where were they?

ZT: Department of Surgery, Harvard Medical School, Boston, Massachusetts.

DWM: Okay.

ZT: Frank, Seligman and Fine from the Surgical Research Department at Beth Israel Hospital in the Department of Surgery at Harvard Medical School in Boston. They would be one for PD. Then I would put Grollman. Grollman. You haven't heard about Grollman?

DWM: This is pitiful. No.

ZT: Grollman was from Texas but I don't remember where from. Right now I don't have time to look at it.

DWM: That's fine. Okay. I'll find it.

ZT: Then Maxwell from Los Angeles. This catheter. This catheter, Maxell catheter.

DWM: Okay.

ZT: Then of course Moncrief and Popovich and Nolph, you know, that's obvious. Tenckhoff of course, you know. It's very difficult. It would be necessary to say many more. Here all these people are in this listed but here on this table is, for instance, who developed what. This is all _____ for instance here _____ whom I consider innovative in peritoneal access.

DWM: Right. Right.

ZT: On this table.

DWM: Right.

ZT: These are _____ of course. Gotch is not very well known but Gotch was the first guy who found that silicone rubber is not irritating that much in the peritoneum as others. Grollman, _____. Gunter is always mentioned that it was the first peritoneal dialysis however Gunter, as a matter of fact, didn't do peritoneal dialysis really, only one exchange, but he is always mentioned. In hemodialysis I would say of course that Able, Roundtree and Turner.

DWM: Right.

ZT: There is no question about it; they thought about almost everything. Then the second would be, I would say still, Haas, Georg Haas.

DWM: Yes. Dialyzed a dog actually.

ZT: Yeah, absolutely. Then Thalheimer, you know, this is the first guy who used the cellophane. Then you have to say Kolff of course and you have to say Alwall, which you didn't know because he's from Europe. Europeans are not that... But Alwall and then I would say hmm...then I have to say that regarding still Kiil, you know, this Kiil dialyzer it is but you have in the middle you know you have here it is everything that is written about these people. But here I mentioned about Haas, _____, Thalheimer, _____. My gosh. I mention a lot of these people. But some of them may be more important than others. Of course, you know Stewart and Mahon from Cordis Dow, this capillary dialyzer of course. But there are many others. It's so difficult to say. I mentioned about Teschan.

DWM: Yes.

ZT: I thought about, you know, that he was really good. If I say actually Haas, Thalheimer, Albert, Kolff of course and then Teschan. Of course Scribner, there is no question about it; he's almost like our God. Scribner was an unusual guy. He was clinical, very clinical, very clinical. He observed the patient and he knew what was going on. We have, for instance, one of these pioneers of daily dialysis was Bonamini; _____ Bonamini from Bologna, Italy. We gave these guys no recognition here during our conference. I will stop on these, okay.

DWM: Okay.

ZT: I can mention about a hundred names.

DWM: A lot.

ZT: But I think that I mentioned the most significant, I think.

DWM: Well I know we're running close on time here but I wanted to just see if you would just say word about what you think will happen with dialysis over the next 10 to 15 years. What do you think might be the big improvements that we would see in dialysis care?

ZT: I think that, of course, daily dialysis, for me, is ... but I think that this will not be for more than 20% of people. The majority of people will be on center dialysis and I'm afraid that we will not do too much better on hemodialysis. I am afraid that dialysis will not be prolonged, you know. You know that I believe that longer dialysis is better and it should be introduced and maybe, but I suspect that it will not be done, unless the patients will see the difference but in the United States I doubt it. I doubt it. But home dialysis may take over really. I don't believe in a wearable artificial kidney, sorry if somebody told you this, I don't believe it. I don't think that this will be available by the end of the first quarter of this century and maybe never. The problem is with blood access. Blood access is extremely difficult _____ for this wearable artificial kidney so I am afraid that it will not. I would say that maybe transplant will be better _____ to manufacture kidneys from stem cells. I think it would be possible. That, I think, would be possible. I don't think that animal kidneys would be really used. They were used and there is something about these animals; I don't know which animals as a matter of fact. But to manufacture kidneys from stem cells...

DWM: Um hmm.

ZT: and discover how to make them, you know, what the stimulating factors and other... you know, this budding ureter which is producing different kinds of stimulating factors and inhibiting factors and so on. But this will not be also in this quarter of the 21st century.

DWM: May still be a ways off.

ZT: I don't know but maybe in the middle of the 21st century.

DWM: Well, I thank you very much for taking your time today.

END OF DICTATION

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DWM/dlb
T: 04/07/09