VOICE EXPEDITION INTERVIEW TRANSCRIPT

Karl D. Nolph, M.D.
Interviewed by Dugan W. Maddux, MD
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DWM: Today is Tuesday, February 24, 2009 and I am with Dr. Karl Nolph in Karl's office at the University Health Sciences Complex in Columbia, Missouri. Dr. Karl Nolph has been a part of the nephrology at the University of Missouri since 1969. He was the long-time Director of the Division of Nephrology here. Dr. Nolph has cared for nephrology patients, particularly peritoneal dialysis patients, during the past 40 years and much of the published peritoneal dialysis knowledge bears his name.

Dr. Nolph I appreciate you letting me come today to talk to you about the history of nephrology and your part in it.

KN: Well thank you for coming.

DWM: I'd like to just start with where you were born and raised and then work to where you were educated, went to medical school and that'll sort of give us some background.

KN: I was born in Brookville, Pennsylvania, February 6, 1937. I went on to Franklin & Marshall College in Lancaster, Pennsylvania where I majored in chemistry and then went to the University of Pennsylvania School of Medicine.

DWM: What year would it have been that you were in medical school?

KN: I graduated in the class of 1963 and started there in 1959. From there I did my training in internal medicine at the Bryn Mawr Hospital, which at the time was affiliated with the University of Pennsylvania. I was then able to move back to the University of Pennsylvania in a Nephrology Fellowship and enrolled in the Berry Plan. During the Vietnam War you could apply for the Berry Plan and if your name was selected by, I think random selection drawing from a hat, then you would be allowed to complete your training in your specialty before you would go into the Army but at the completion of your fellowship you were obligated to go in. I was lucky enough to get that and then didn't know where I was going as my fellowship was drawing to a close. One day Bill Blumley came into the dialysis unit and said, well where are they sending you. And I said, I don't know, I haven't heard yet. So he said, well let me make a phone call. So he came back, probably less than 15-20 minutes later and he said, you're going to Walter Reed. And I said, oh really. And he said, yes I called Colonel Paul Teschan and told him that you had this great interest in peritoneal dialysis and it so happens that Paul Teschan is looking at the effects of uremia on the nervous system of monkeys. He ligates the ureters and he needs someone who can keep them alive with peritoneal dialysis. So he said, that will be one of your

assignments. So sure enough it wasn't long til I got my orders that was going to the Walter Reed Army Institute of Research and I also had a clinical assignment to the Walter Reed General Hospital. I went there and had a marvelous time doing peritoneal dialysis research and working with a number of people who were assigned there at the same time. Bob Schrier was there, Mike Dunn, Craig Tisher, we were all there together. Many years later when Bob Schrier was President of the ASN he got that group together to form the Program Committee for that year for the ASN so it was the old Walter Reed group recombined. We did a lot of sharing of our thoughts and ideas and people like Bob Schrier even collaborated with me on a few peritoneal dialysis papers. He hadn't known that much about peritoneal dialysis before but he really enjoyed the studies that we did. He said, what I like about this field is, he says, you and I are the only guys in it. His main interest at the time was in factors affecting urinary sodium excretion, third factor and the search for natriuretic factors and this kind of thing. He'd spent some time working with deWardner so this was a deviation for him from his usual practice. Bob Schrier was out looking for positions and he came back and said, why don't we go somewhere together. So I said, well it sounds good to me. He said, I've looked at the University of Missouri and why don't we go there together. I said, well let me go take a look. So I made a trip out here and I liked it very much. I said, sure let's go. Bob was a little senior to me and he was considering coming as a Division Director and I would be his colleague in the faculty but at the last minute Larry Earley convinced Bob Schrier to go to California instead. But I, meanwhile, was very much intrigued with coming to the University of Missouri. When Bob decided to go elsewhere then the Chairman here, Charles Mengel, began to recruit another Division Director and he ended up recruiting Jack Maher to come as the Division Director. I knew Jack very well because while I was at Walter Reed he would occasionally come over for conferences, the Georgetown group. When I had applied for fellowships I had applied at two places, Georgetown and to University of Pennsylvania, and I had met Jack when I made my visit there. I was accepted at both places and Jack always accused Marty Goldberg and the group at Penn of somehow cheating when they recruited me but he was glad we could be back together and we had some good times here. He left in 1974. He and his wife were eager to get back east where they had friends and family and he went to Connecticut and I became the Division Director at that time. So that's maybe more than you want to know about my education and how I got here.

DWM: That's perfect. But I don't want to get too far away from that without figuring out where your wife, Georgia, entered the picture since she's also a physician. So how did you all meet and where did your paths cross?

KN: Yes. I was in the second year of medical school and I belonged to the medical fraternity Phi Rho Sigma and many of us from Franklin & Marshall went to Penn. I think there were like 16 or 17 of my classmates that all went to Penn to medical school. We found this boarding house where we could have rooms and so my roommate, he also belonged to Phi Rho Sigma, and he said they're bringing some girls over from Women's Medical tonight and a friend of somebody's is bringing some over. I said, I can't go I have to study. Well let's just walk over, it's just across

the street and so and so has this friend and she's bringing some friends and some of them are the new freshman. Oh, I'm sorry and I just insisting I couldn't go. Finally with a lot of arm-twisting I said, okay. I went over and when I walked in Georgia was playing the piano and people were gathered around singing. Then I went up afterwards, started talking to her, ended up taking her home and we started dating almost constantly after that and it was only the next summer then that we were married.

DWM: Was it difficult at all coordinating her finishing medical school and your finishing training? I mean it's…

KN: No we had many study dates while we were in medical school and we enjoyed that. Then we felt that getting married was a big advantage because now we shared an apartment and could study right there; didn't have to decide whether we were going to study in her library or mine at which medical school. She was at Women's Medical School, which is what it was called at the time. So we just worked it very well. In her senior year in medical school that's when she got pregnant with our daughter Erika. Erika, who is now a Professor here in the Department of Family Practice and Director of the Residency Program. My wife, Georgia, timed it very well because her last rotation her senior year was OB/GYN and she just finished the last rotation and I think it was like two or three days after her last rotation she delivered Erika and then there was something like a couple of week interval before graduation. So she was just fine for graduation and then started her internship right on time.

DWM: Wow. Well that is good timing because it's very difficult, even today I think for women physicians…

KN: Oh yes.

DWM: in training to figure out how to deal with pregnancy and _____

KN: Well we found a wonderful lady in Philadelphia who would come in the mornings and take care of Erika. If we were both on call the same night she would bring Erika over to the hospital and prop her in her child seat right in the middle of the table where the house staff were eating. So it worked out very well.

DWM: I guess no wonder Erika is a professor _____

KN: That's right. That's right.

DWM: She just started out that way.

KN: That's right so we were very fortunate to have good help to get through those years.

DWM: What was it about your residency that made you interested in nephrology?

KN: Well when I was a resident in internal medicine at Bryn Mawr I worked very closely with the nephrologist there, Dr. John McGhee, and he had trained at Georgetown and that was my early link to Jack Maher and George Schreiner and one of the reasons I visited there was at his encouragement to do so. But he was very much into peritoneal dialysis. In those days there were very few hospitals that had hemodialysis so the only thing we could offer in those days, back in the early 60s, '63 through '66 when I was a resident, was peritoneal dialysis. We would do a lot of peritoneal dialysis for acute renal failure, nothing for chronic. There wasn't much to offer for chronic renal failure patients at that time. But I got very interested in peritoneal dialysis and he taught me to insert the stylet catheters and pretty much get it going. He would often kid that he was putting himself out of business because he'd taught Karl to do this and he was afraid he wouldn't be consulted any more. But that was really the start of it. Then when I went to my fellowship Lee Henderson was there of course.

DWM: Right.

KN : And Lee was very much into peritoneal dialysis research. I got involved with Lee Henderson in studying peritoneal transport and we were very interested in the effects of hypertonic solutions on the peritoneal microcirculation. We published a paper in *JCI* showing that exposure to hypertonic peritoneal dialysis solutions seemed to transiently increase clearances and we wondered if it was a vascular effect, vasodilatory and then when you went back to the less hypertonic that would disappear. This then led to my future interest in studying all kinds of vasodilators and what effect they had on peritoneal clearance and peritoneal transport. In that same set of studies we just happened to have all of the electrolyte concentrations in the drainage and in the patient's serum and that's when I first noted that the ultrafiltrate had a lot of electrolyte-free water compared to the extracellular fluid. That led me to sit down and reanalyze that data when I got to Walter Reed and this is where I came up with the concept that there must be some kind of sodium sieving going on in the peritoneal membrane. There had been a previous explanation circulating around written in the *Annals of Internal Medicine* by Dr. Frank Epstein that proposed that the reason patients on peritoneal dialysis with aggressive ultrafiltration develop severe hypernatremia was because they got hyperglycemic, this led to mobilization of cell water, this led to a drop in serum sodium concentration and inrush of sodium from the dialysis solution and then when the hyperglycemia disappeared and the glucose went back into the cells so did the water and you're now left with all that accumulated sodium in the extracellular fluid space and hypernatremia. I wrote the paper saying this can't be. First, of all you see hypernatremia without hyperglycemia developing. Secondly, you can see the hypernatremia without any drop in serum sodium having been obvious at anytime. Thirdly, if you look at the dialysate drainage, sodium is always removed, it's not taken up, there's always net removal. I said, what's happening is water is being removed without sodium compared to the concentrations in the extracellular fluid space. I proposed a concept of a sieving coefficient and published this in a

paper I submitted to the *Annals of Internal Medicine*. One of the reviewers came back and objected that it would be impossible for a biological membrane to sieve sodium; that there was no way this could happen. He said we know this from our experience with glomerular capillaries; that the filtrate has essentially the same content as the extracellular fluid with _____ and that sort of thing. But he said, we know that biological membranes could not sieve sodium. I rebutted and said, well I don't think there's any other way to explain the observations and what holds true for the glomerulus may not hold true for the peritoneal capillaries. So that was the beginning of the concept of sodium sieving back in that era of '67 is when I was working on that.

DWM: Right.

KN: Far before we knew about aquaporins.

DWM: We've come a long way, yes we have.

KN: That's right. That's right.

DWM: Before we leave I want to take you back to the 1963, 1964 where you're there at Bryn Mawr seeing acute renal failure. Not chronic renal failure.

KN: Right.

DWM: Acute renal failure being treated by peritoneal dialysis. Can you tell me a little bit about what was the procedure? If a patient came in, what kind of condition were they in? When did you all decide to dialyze them? What did it take to actually put someone on peritoneal dialysis at that time?

KN: Right. These were often the ill patients in the ICU, patients who'd experienced prolonged severe hypotension, septic patients, postop surgical patients and the hope would be that if we could provide some sort of control of their electrolytes, acid-base, potassium, BUN there might be hope that they would open up and diurese and we could get through this. Many times the triggers were uncontrolled hyperkalemia, real high BUNs, what was thought to be impending uremic symptomatology, acid-base problems that weren't being controlled readily and then, of course, fluid overload; just getting some of that off with peritoneal ultrafiltration. In those days we had 7% solutions. Those were the hypertonic solutions. You had 1.5 and you had 7%.

DWM: 7.

KN: So when you used 7% you really ultrafiltered. Those studies that I did at Penn when I was a fellow they were with 7% so you really saw the sodium sieving when you used 7%.

DWM: I'm sure.

KN: And could pull off a liter of UF in an hour or so. So that's when we did it. At Penn it was pretty much the same thing. We did a lot of peritoneal dialysis to try and treat the acute renal failure and they had, I think, several hemodialysis machines in what was the beginning of their chronic hemodialysis program. When I got there I think the total number of patients on chronic dialysis that Lee Henderson and Bill Blumley were following was something like three and that was it. They were saturated. The pressures to put more people on were tremendous. I can remember an instance where some very wealthy man had a young wife with chronic renal failure and uremia and he offered to build them more dialysis facilities and buy them more machines. The philosophy at that time in most academic centers was, you know, we cannot take on a chronic renal failure population. We need to have a few machines so that we can study this form of treatment but we really can't become a service-oriented institution. There was a lot of that feeling among academic nephrologists everywhere in the early days of dialysis; that the goal of the academic institution is, yes, to help improve dialysis and to study it and to hopefully prepare it for some day where it could become a widespread clinical service but if we take on widespread clinical dialysis services our academic missions will be destroyed. That was the philosophy at the time. So as a fellow I had to watch very otherwise treatable young dialysis patients die because there was no place for them in the program. I remember a young man, the same thing, the only answer was, sorry we're full, we have no room, we have no capacity to help you and we'll keep you as comfortable as we can. So we relied a lot on peritoneal dialysis for acute and we had a few stations for the chronic dialysis. The transplant program was just beginning when I was a fellow and of course it was felt you also needed to keep the machines available for the immediate post transplant period when you might need to do dialysis. At that time they were doing all live donor transplants at the University of Pennsylvania so a rapid diuresis post transplant was very common and often it was massive. Jay Puschett was a fellow with me. Jay's had a long and stellar career in nephrology. Jay and I would take turns sitting up at nights with these diuresing post transplant patients. Often the diureses were, you know, a liter or more per hour. We had one patient I think that put out 21 liters in the first 24-hour period. So we had to sort of rewrite the IV orders every hour on the hour. We would get stat urine electrolytes, see what was coming out, look at the total volume, what was in it and write an IV to try and keep up. We also did a study, which was published in the *New England Journal* looking at the mechanism for this massive diuresis. There were those who felt it was all just fluid overload and you should let it happen and there was those who felt, no, no in the immediate post transplant period of a live donor transplant there may be some tubular abnormalities. So with Lee Henderson we designed a protocol to very carefully replace every milliequivalent of sodium and chloride and every drop of water that came out as best we could measure and see what happened if we maintained a constant volume status. For example in, I think, three or four patients that went into the *New England* paper study the diuresis cut back. We noted that the diuresis was associated with indices of proximal tubular malfunction in the early stages, a lot of glucosuria. As the glucosuria disappeared so did the diuresis. So indeed it may be volume mediated in some patients but in those particular

instances we felt their volume status was optimized at the beginning of the diuresis. We didn't obviously maintain somebody in obvious overload. We got them where we thought they were optimum and kept them there and the diuresis did cut back. So that was another one of my very first papers and that was in the *New England Journal*.

DWM: Yep.

KN: With Jay Puschett. You've probably heard of Jay Puschett.

DWM: I have, yeah. I wanted to just talk a little bit about the nuts and bolts of those early peritoneal dialysis patients both at Bryn Mawr and U. Penn; acute renal failure, early PD patients. What catheters were you using? What would the regimen have been like? I gather there were commercially available fluids.

KN: Yes.

DWM: You were not mixing your own dialysate I suppose.

KN: No. No.

DWM: So what catheters were you using and how were they inserted? What kind of procedure was that?

KN: Sure, I'll tell you about that. I'll just mention one thing that might interest you though. In hemodialysis in those days Bill Blumley was one of the folks who had conceived of the coil dialyzers.

DWM: Yes.

KN: And we would roll our own coils.

DWM: Do you remember that? What was that like?

KN: Oh we did that. We bought long strips of cellophane and they had this mesh and we would stretch it out on the floor.

DWM: On the floor?

KN: You'd stretch out the mesh and then you'd stretch out the long cellophane, you know, 20 feet long or so and then you'd just roll it up. Then you would attach the tubing so the solution could flow through and it was quite the thing.

DWM: So every time you were doing a hemodialysis you would hand-roll a new coil for that.

KN: Yes. Oh yes. And the fellows had to take turns being dialysis technicians. They had dialysis technicians but they thought every fellow should have a rotation as a dialysis technician. And we were using the old tanks. The twin coils in the tanks. Then we went to the recirculating single pass, which was a big, big step forward.

DWM: Tell me about the recirculating single pass. Tell me what that meant.

KN: Well the dialysis solution would just keep coming up through the coils and then just keep recirculating and recirculating in the tank. It wasn't just run through one time and discarded like it had been. Then the blood path, of course, was through the tubing. But we used the coils. Now Bill Blumley, at the same time, was working on hemofiltration. He and Lee were very interested in hemofiltration at that time. So part of my work was to be involved in helping them a little bit with that but I gravitated towards peritoneal dialysis much more.

DWM: With the hemodialysis that you were doing there at Penn, were you all also, as the renal fellows, putting in the access or where surgeons doing it?

KN: Well that's interesting too. Jay Puschett and I were taught by Lee Henderson to put in the Scribner shunts so part of the fellow's job was to do the surgery and put in the Scribner shunts right in the dialysis room. Jay and I got fairly good at it and one time Lee was off somewhere, he was the attending but he came back and he was surprised because we had the patient with the shunt in place and on dialysis. In fact when I went to Walter Reed one time they needed somebody to come over to the Naval Center, Bethesda Naval Medical Center, and they needed a Scribner shunt placed. I guess they couldn't find anybody that had done it so I went over there and put in a Scribner shunt as a consultant from Walter Reed to the Bethesda Navy Medical Center, which is interesting.

DWM: Do you remember enough about that procedure that you talk me through what it took to actually put in a Scribner shunt?

KN: Well you, of course, had to cut down on the radial artery and vein and you would just have to tie off the artery so you could slip in and then snug the loosening tie, slip it in, tie it around then have your arterial port. Then on the venous side you would just have to cut down on the vein and put the other end into the venous side with the little plastic tip and then you would close it up around it and of course the plastic loop would be external and you could disconnect the plastic loop and have access to the artery and vein that way. It was sort of just a complicated cutdown really with two vessels.

DWM: How did the patients do on hemodialysis, those early patients? What kind of treatment were you doing? What length of treatment were you doing and how did they tolerate it?

KN: Usually they would have about, as I recall, a six-hour treatment three times a week. There were often a lot of side effects with the dialysis. The clearances with those old twin coil machines were quite good so, you know, disequilibrium and symptoms but many of them tolerated it very well. These were the chronics.

DWM: Right.

KN: For the acutes were mostly PD.

DWM: Yeah. Okay.

KN: Yeah, the acutes were mainly PD. Now back to your…you wanted me…

DWM: Yeah. Yeah.

KN: I didn't mean to deviate from the…

DWM: No. _____

KN: Back both at Bryn Mawr and Penn we used the very hard stylet catheters and these would come and you'd have to do the puncture and with the stylet and the catheter would be on the outside of the stylet and you'd puncture and then you'd slip the catheter down in.

DWM: This would be a fairly short straight catheter _____?

KN: Yes. Short and straight. And often you would just put the very tip of the catheter into the peritoneal cavity and then instill a couple liters of fluid so hopefully the loops of bowel would float away when you then made the puncture and slipped the stylet in. The incidence of rupturing the bowel wasn't very high unless a patient had a lot of adhesions and then it might be that it couldn't float away and it would be locked in and you would easily puncture it. Occasionally bowel punctures would occur and you'd drain back feces. Occasionally it wasn't unknown to hit the aorta. That wasn't very good. But then you'd usually just leave them in for the period that you did the peritoneal dialysis treatment and that might be for 24 to 48 hours. The nurses would use solutions in bottles and they would run it in and then drain it and then hang some new bottles and run it in and drain it.

DWM: What kind of dwell time were you using?

KN: Usually hourly.

DWM: And how did you come up with that dwell time?

KN: It had been a tradition for a long time to use the hourly and Fred Boen had published his classical little paper showing that clearances at one hour were pretty good and I think a lot of the thinking was based on Fred Boen kinetics and I think that's pretty much what they used so it was very much traditional to use hourly exchanges. Just instill as fast as you could, leave it in half an hour and then drain over 20 and then it'd be about an exchange every hour. Then run for 24 to 48 hours and take out the catheter because the feeling was if you left it in the patient might be uncomfortable especially if you drain the abdomen and then the increased risk of infection, the exit site was just wide open with this thing through the hole. Exit site bleeding with the catheter puncture was such a challenge and many of us developed all kinds of maneuvers to try and do that. We would, of course, maybe use some epinephrine in our lidocaine and make a great big lidocaine bee hive where you're going to put in the catheter and not only have it numb but have a lot of epinephrine there for vasoconstriction. You'd still often get bleeding and so I often found that topical fibrin; if I would just, with a Q-tip, pat some topical fibrin on there when it started to bleed. Because if you didn't get that bleeding under control some of the bleeding at this puncture site could trickle into your solution and the solution comes out looking bright red and all it took was a cc or less of blood in the drainage and you think you're having a massive hemorrhage. It was very disturbing to the patient and the nurses to have bloody looking drainage so I liked to get it really dry so you had crystal clear fluid coming out.

DWM: Right.

KN: But those were the days of the stylet puncture and that's what we did at Penn as well.

DWM: Penn as well.

KN: Sometimes when you would go to remove the stylet catheter the omentum would be locked in the holes. They would have just been sucked into the holes. I can remember one time as a fellow I pulled out the catheter and the omentum came right with it so Lee Henderson happened to walk by. I said, what do we do here? He said, I'll show you. And he put on a pair of gloves and he just scraped the omentum off the catheter and stuffed it back in and everything was fine so we didn't have to do an omentectomy, just put it back in.

DWM: Just back through the hole.

KN: Right. Right.

DWM: Which brings me to talk about… I mean, you know, there were things that you all were just changing by experience. Like, well here's the omentum, what do you do? There's bleeding at the exit site; how do you treat that?

KN: Um hmm.

DWM: Would you have thought of peritoneal dialysis, at that time in the mid 60s, as sort of an established procedure or an experimental procedure? I mean these were people who were quite ill anyway and without dialysis, might have died or would have died.

KN: Right.

DWM: Did you consider it a proven therapy or an experimental therapy?

KN: We felt that it was a widely applicable therapy for acute renal failure for controlling volume problems and so on in situations where there was acute renal failure. I think that many of the nephrologists around the country were being trained to do peritoneal dialysis for that kind of situation. There was almost no chronic dialysis when I was a fellow. Penn had the two to three patients that I mentioned. The Seattle group was just getting started and they, of course, had the Scribner shunt and were doing some center hemodialysis. Fred Boen and Henry Tenckhoff were developing peritoneal dialysis there as an actual chronic kind of thing but I think most people considered that very experimental at the time. Fred Boen started taking the great big carboys full of fluid to the home and doing peritoneal dialysis in the home and teaching the patients to do it. So those things were just being talked about. Even in Seattle they still had the committee to decide who would go on dialysis and who wouldn't.

DWM: Right.

KN: Just like Penn. They may have had more slots than Penn did but they had a limited number of slots and so there was the so-called death committee that would evaluate which patients should go on to their openings and which patients should be rejected.

DWM: Was that happening at Penn also? I mean how did _____

KN: At Penn it essentially was a situation where they were full so there were no new positions so nobody could be accepted until a slot opened up and then if one of those patients died a slot opened up they could take somebody. They'd probably take somebody in house that was just a good candidate because the other people would be long gone you see. So they'd take somebody on hand. But it was just a matter of a slot opening up by death and then allowing them to take on another person.

DWM: How long were those three who were on the chronic dialysis; were they surviving very long?

KN: Yes. Some of them had been on for years. Some of them had been on, I think, for several years when I got there. One was a professor from Jefferson Medical School, a pathologist, and

he'd been on for some time and he was very interested in doing research on himself while he was on chronic dialysis. He was very interested in the darkening of the skin in chronic dialysis patients.

DWM: Um hmm.

KN: And what that might be. He was doing a lot of studies on his own skin. He was very alert and very hard working and would work while he was on and he'd been there for several years.

DWM: Yeah.

KN: Many of them… You know the transplants they also, as I recall, needed to keep a machine available if somebody was being worked up for a transplant but again that was usually a live donor situation, worked up as they were approaching so they wouldn't have to be maintained on those scarce spots very long.

DWM: Yeah. When you went to Walter Reed I was interested that you had worked with Paul Teschan.

KN: Yes.

DWM: I interviewed Dr. Teschan and of course he had this marvelous history of having been in Korea.

KN: Oh yes.

DWM: And running the hemodialysis unit there.

KN: And then he was in Vietnam.

DWM: Yeah. He didn't talk as much about Vietnam.

KN: Yes. But in Korea, you know, he had wonderful photos of what they did there.

DWM: Yeah. They were doing hemodialysis in the evacuation unit there in the field.

KN: Right. Right. Right.

DWM: It sounded like it was very dramatic.

KN: I think they used the old Kolff rolling drum kind of dialysis machine. Yes. In Vietnam, again, the frustrating thing was that so often they were able to prevent uremic death, death

from hyperkalemia, fluid overload but in the war zones there were often so many other complications that came along and especially then infected wounds and so on which resulted in about the same mortality. It may have taken a little bit longer but many of the studies done in those particular areas didn't show much of an impact on overall mortality.

DWM: Yeah.

KN: It changed the mode of death.

DWM: Right. Speaking of infections, when you were in your residency and fellowship and doing this acute peritoneal dialysis, were infection, peritonitis, was that a problem or was the catheter in and out so fast that_____

KN: Yes the catheter was in and out so fast that we usually were able to get and out and do peritoneal dialysis without peritonitis. In my experience it was a rare, rare thing to have peritonitis with that kind of in and out.

DWM: Yeah. And what if you did 48 hours of peritoneal dialysis, pulled your catheter and you still had renal failure for another few days after that. I mean, was a second chance…was there an opportunity to reintroduce your stylus in a couple of days?

KN: Oh yes. Often we were… Oh sure. Oh sure. We would often then repeat but the idea was to get in and get out and maybe do that once a week and just keep doing it as necessary. I can remember a young woman at Penn who had acute renal failure following a severe bout of gastroenteritis.

DWM: Hmm.

KN: We dialyzed her for quite a while and she basically opened up.

DWM: Well then that takes us to finishing up at Walter Reed.

KN: Yes.

DWM: And coming to Missouri. So what was happening in the Division of Nephrology here when you came?

KN: Well Jack Maher and I arrived. I actually got here, I think, July 1st and he got here August 1st.

DWM: And what year would that have been?

KN: That was in 1969. 1969. We ordered some hemodialysis machines.

DWM: So there was no hemodialysis here at all.

KN: No hemodialysis but I started doing peritoneal dialysis right away in acute situations.

DWM: Had they been doing PD here before that then?

KN: Yes. Yes. So they had the catheters and everything that I was used to using. So I could jump right in and continue the same practices that I had followed in my residency and then in nephrology fellowship and at Walter Reed; stylet peritoneal catheters. The Tenckhoff catheter was…we were hearing about that and I don't think it was too long…I'm trying to recall when we first used them here because we really didn't get into chronic peritoneal dialysis in a big way with the automatic peritoneal dialysis machines and IPD. And in fact I think we mainly launched into our chronic peritoneal dialysis program here when we started in CAPD in 1977 so that was almost eight years where we were doing some chronic hemodialysis with our machines, acute and chronic, not very many chronics.

DWM: About how many do you think it was?

KN: I think when we first started, again, we're talking about a handful or less at the most. And Jack Maher also came from that school of thought that academic centers needed to do hemodialysis for training purposes and for research purposes but service would kill the academics and you had to keep it under control and not expand it. So he wanted hemodialysis being done, he wanted peritoneal dialysis being done for training and research purposes but that was the philosophy that many…

DWM: Was the perception that chronic hemodialysis was an okay thing but it just needed to happen outside the academic centers and…

KN: I think that was the philosophy that was emerging as more and more successes were being reported from Seattle. That it could be done. But I think the big debate was where should the majority of the service be provided. Should it be provided by academic centers or by private nephrologists working out of dialysis clinics and this sort of thing?

DWM: Were you all seeing any private dialysis clinics in this area? I mean were people coming in to provide that service?

KN: Not really at that time. Not really. So eventually we got into more and more of the chronic and then in 1974 when I became Division Director we had established some chronic dialysis. We had an old building out behind the hospital. During the war and right after World War II there were many, and maybe the Korean War too, there were many GIs that could now

go to school with the GI Bill. They put up all these temporary dormitories and those were behind the hospital so we had one of the old dormitories where we had our chronic hemodialysis unit. In 1974 when Jack left and I became Division Director, that's when I recruited Dr. Van Stone and then he took on the responsibility of developing a chronic hemodialysis program out of that old building.

DWM: What changed your mind? What changed your philosophy from that academic centers don't need to be involved in this to saying well we've got to create this program?

KN: Well I think that more and more young nephrologists felt that we needed to offer that, especially if it wasn't being offered elsewhere. I'm not sure I can answer your question exactly. I always, once I even was a resident, had a tremendous interest in dialysis so I didn't have a fear that dialysis would destroy academia and in fact that's been a major area of interest. Now many people would argue that at the University of Missouri we were so dialysis-oriented in our research and our teaching and our focus that we didn't do enough in basic renal physiology, we didn't do toad bladders, we didn't do micropuncture and so in the eyes of some people we would have been a weaker nephrology program because we weren't involved in that very basic kind of renal physiologic research. The programs that were being run by the Don Seldins, Brenners, Rectors, I mean these were high-level renal physiology programs and to those kind of people that dialysis was a distraction from their true love which was renal physiology and applications of renal physiology to understanding clinical nephrology but not doing dialysis. And clearly in those days the dialysis interested people were considered second-class citizens by the others.

DWM: I heard that a bit that the early dialysis people were just sort of considered tinkerers.

KN: Yes.

DWM: And procedure oriented and not true scientists, that there was_____.

KN: Well I think this is why ASAIO was formed, to find a home for people who were interested in artificial kidneys and dialysis in general and they didn't feel at home at the other nephrology meetings and so ASAIO filled a big need. And then our Annual Dialysis Conference stepped in and filled that need. It's a gathering place for doctors and nurses who have a major interest in dialysis, not only from a clinical point of view but from the standpoint of their own research and scholarly thinking. But still I think there's that division; the ASN and the NKF, they want to be careful not to have too much dialysis so I think in that way they're very happy that we offer this huge forum for all these dialysis papers; two and a half to three days of nothing but dialysis and hundreds of presentations that probably would not be welcome at those meetings where they want to make sure they have a balance of the whole world of nephrology and not just dialysis. But when you limit it like that it limits the dialysis people to have all the voice that they feel they need.

DWM: Yes. Well and having been to your annual meeting, I mean, it's very scientific, it is and it's interesting to hear the, sort of, dichotomy of thought between the two groups.

KN Yes. Yes.

DWM: Because I see the annual dialysis meeting as being a very scientific meeting.

KN: Well we expanded then and John Van Stone did a marvelous job of expanding our chronic dialysis program. We may have had, I can't even recall. We may have had a few patients on cycler PD and of course we were hearing great things from Toronto about Dr. Oreopoulos and his IPD program.

DWM: Yes.

KN: We had a few of those cycler machines but then we got very much involved in our own peritoneal dialysis research and it was often done though with still the manual PD. Much of the vasodilator work, much of the work on transport that I did in the early days, sodium sieving, all done with manual PD in the usual way and looking at the drainage and many of those studies were done in our clinical research unit doing PD up there.

DWM: Yeah.

KN: But the CRC nurses were well trained in doing it and collecting the samples and using exchanges with and without vasodilators like nitroprusside and that sort of thing. Then I had a number of NIH contracts to study peritoneal transport in that way. That's how I got to know Jack Moncrief and Bob Popovich because they had interest in peritoneal dialysis transport. Bob Popovich had even come up and helped to act as a consultant for some of the engineering problems that we wanted answered relative to some of our peritoneal dialysis research so he had been a consultant on some of my early… I think on one of my VA grants that he could act as a consultant from an engineering point of view. So that's why we had a relationship before they conceived of their idea in 1975. Then once they conceived of that idea and we talked about it and we decided to join in and evaluate this way of doing PD, that's when our PD program really took off and began to expand.

DWM: Yeah. Well tell me about those early collaborations with Moncrief and Popovich and what you were doing to move that forward.

KN: Well we shared a great interest in peritoneal dialysis. They had NIH contracts and we had NIH contracts and so there'd be the gathering of the contractors meeting at NIH and people would get to know one another. They would talk about their work and we would talk about ours and I mentioned the collaborations. Then they, in 1975, had this patient that…I forget all

the circumstances but they decided to send him home and just let him do peritoneal dialysis manually with long dwell exchanges around the clock and it worked very, very well. They submitted an abstract to ASAIO and I'm sure you've heard about this but they had a very long title and I can't remember what it was. It was like slow equilibrium peritoneal dialysis or something like that and it was rejected. I think people looked at the title and when they read it they weren't quite sure what it was all about. I thought it was a very exciting concept and I remember we sat down at a contractors meeting and we were discussing how exciting it was. It was a way of providing a continuous dialysis therapy with steady state chemistries and gentle steady UF and all these advantages and we were so excited about it. At that discussion we were trying to think of a name that would maybe help people understand and we all threw in words and somehow out of that meeting we came out with the fact that, well it's continuous, that's a key word and it's ambulatory, they can do it wherever they happen to be, it's peritoneal dialysis. Then I think we thought there is COPD, chronic obstructive pulmonary disease, and everybody likes that, COPD, so how about CAPD and so we kind of stepped back from the table and say, eureka, you know. So then we did our collaboration and NIH was very interested in what they were doing and they added this on to one of their contracts to evaluate this technique further. Then we were invited to join in with them and so we did that; Austin Diagnostic Clinic and University Missouri as a collaborative study and I think we then published our paper in the Annals with nine patients and all the results and used the term continuous ambulatory peritoneal dialysis for the first time. That really seemed to catch on; that people then got interested in it. Other people then thought maybe that would be a worthwhile thing to try.

DWM: With those early CAPD patients, that first study, what catheters were you using?

KN: We, at that time, were using the Tenckhoff catheter.

DWM: Tenckhoff.

KN: So we had gone to the Tenckhoff. We didn't have all of the catheters that Dr. Twardowski invented yet.

DWM: Right.

KN: And they worked very well and one of our surgeons, Dr. Kirt Nichols, in very early years started working with us and he's still with us putting in catheters and he takes it very, very seriously. This is so important to a program to have a surgeon that really cares and really doesn't look at this as something you quickly assign to your first year surgical residents, you know, and treat it like a cutdown. He does them and does them very, very carefully.

DWM: The NIH; who at the NIH was sort of the champion of this? It sounds like they were pretty easy to work with.

KN: Well Ben Burton was very interested in this and he helped and Fernando _____, he's now deceased, and then Nancy Cummings came along. But in the beginnings it was Benjamin Burton and he was very intrigued by this idea. I think at the contractor's conference they developed more and more of an interest in this. They wanted us to expand our studies and they were very interested in us evaluating different numbers of exchanges per day; four, three, five. We wanted to see if we could get solutions in bags because by this time. I should back up and tell you, and it's in this memoir that I wrote, that one of Dr. Oreopoulos' fellows, Jack Ruben , wanted to spend a year with us. He came here and we were just getting into CAPD. So he happened to go back to Toronto to visit with Dimitrios and he told them about this and he said you should try this. So he convinced Dr. Oreopoulos to give it a try. Well when Dr. Oreopoulos decided to give it a try he had solutions in bags. So he said, I don't need to constantly keep connecting and disconnecting the tubing every time I do an exchange. I can just run it in and roll up the bag and then drain into the bag and just spike a new bag. So he developed the bag technique before the Y. It was just simple but it reduced the number of connections and disconnections and so on and could keep the tubing. We had to change the tubing so often and so we then went to NIH and said can you help us get bags. Apparently there had been applications to have IV solutions, all kinds of solutions, in bags in the United States for years and it had always been turned down for some reason.

DWM: Like by the FDA?

KN: Yes, by the FDA. By the FDA. So we went to NIH and said we need to have permission to get solutions in bags and we need some industry to agree to make them. So Ben Burton said, okay let's have a meeting. We had gone to many companies and Baxter was the one that said they'd be interested in looking into this, providing peritoneal dialysis solutions for us and delivering them to homes so people could do it. The others that we went to said, no, no, not at this time. So we had a meeting at NIH and representatives of Baxter came and then the NIH folks were there. It was interesting that we had to have industry but there were all the concerns about NIH meeting with representatives of any company so the Baxter folks had to sit out in the hall and we would run messages back and forth. It was the strangest thing. But finally NIH said we will do all we can to see if we can get at least an investigational new drug application to go through so that Baxter could make solutions in bags and then they could provide these for these patients. We said it would be much safer, the infection rate will probably be lower all of this; it's a wonderful thing to do. So we went to the effort of developing an investigational new drug application and submitted it to the FDA. The NIH gave the blessing. We were waiting and waiting and then we heard from the FDA that there was no need for the investigational new drug application, they were going to go ahead and approve solutions in bags in general so we would be covered under that. They weren't going to do it just for PD but they were going to go ahead. After all these years they were now willing. So we said, great. And they said, it's just a matter of a few signatures. So we waited and waited and waited and I would call and there would be people to tell me, well yes, yes, it's moving right

along, we just need this signature and this signature. We'd wait and we'd wait and we'd call. And finally I called one day and I don't know this woman but I guess it's all right to put the name in your interview. But they said we need one more signature and I swear my memory is they told her name was Mary Fiasco. And I said, well where is she? Well she's on an indefinite leave of absence but as soon as we get her signature. So I said, this is ridiculous. So I called the FDA and I said I want to speak to a medical director. The secretary said, oh you can't just call and ask to speak to a medical director. And I said, oh well I think that a lot of people are going to get unnecessarily ill, they'll develop infections in their abdominal cavities and they might even die if you don't allow me to talk to a medical director. So just a few minutes later she said, well I see what I can do. This guy calls and I don't remember his name but he was very nice. He said, what's this all about? So I told him my name and what it was about and it was an amazing coincidence. He said, would you believe I am just sitting here now reading your paper in the *Annals* about CAPD. I said, well look here's what's happened, it's been approved and for weeks we just need one more signature, one more signature, one more signature and now the signature that we need is from somebody who's on an indefinite leave of absence. He said, I'll take care of this. Low and behold we got a call, like in 24 hours, saying okay you can go ahead, it's approved, solutions in bags. Baxter had already produced them and they had them sitting in a warehouse over in St. Louis and they flew over some bags. I mentioned in here that one of Bob Longnecker's patients from New York had heard about CAPD and he was very interested in going on CAPD. He had come out here and he wanted to be one of the first to go on and he wanted to do it with the bags when they were ready. So he flew out from New York and the bags flew in from St. Louis and we had…this is the first instillation from a bag in the United States. That's the patient from New York and that's the staff gathered around it and this is me right there, that's Barbara Prowant and that's Jack Ruben who had come down from Canada and that's the patient. So we took a picture as the first, as far as we know, the first instillation of peritoneal dialysis solution from a bag into a patient in the United States and I think that was October '78 or something like that. So that was a big event.

DWM: That was a big event. Do you think that Baxter realized how big this was, this start of…

KN: No. We, from the University of Missouri, had approached many of these companies including Baxter and even from Baxter we first got cold shoulders about, would you be willing to make peritoneal dialysis solutions and develop a home delivery service and then eventually we talked about the bag thing with Baxter. But there was sort of a ho-hum, ho-hum, well maybe, maybe we'll see. But then there was one of the executives up there that it caught his attention and he really pushed it through the others. He said you're missing a big opportunity; this could be big. So eventually he convinced Baxter to get into the CAPD solution provider business.

DWM: Because Baxter's been synonymous with PD for a long time.

KN: Yes. For a long, long time. They sort of controlled the market until when Fresenius bought National Medical Care Facilities then they controlled all those facilities and of course Fresenius is in the solution business now as well.

DWM: Right.

KN: So it's not a monopoly by any Baxter any more but they were the first to be willing to jump in and to help us and even there it took a lot of pressure and finally convincing somebody that maybe they should do it and they he had to twist a lot of arms. But often these kinds of processes are drawn out and painful but eventually you get there if you're persistent.

DWM: It does take a lot of patience and persistence.

KN: Yes, yes.

DWM: Did you imagine, in 1975 to '78 when you are beginning to collaborate with Moncrief and Popovich and beginning to look at the Tenckhoff catheter and bags for peritoneal dialysis, did you envision the size of peritoneal dialysis programs and the popularity of peritoneal?

KN: Many people in the early days were predicting what percent of the dialysis population would end up on CAPD and Dr. Oreopoulos was, as I recall, throwing out some pretty high percentages and this would be met with different reactions. There were some people who were skeptical. There were some people who thought, well maybe, and there were some people who were clearly threatened by this. Of course the hemodialysis community… Now we had many private dialysis facilities, there were many people with personal and financial investments in the hemodialysis industry and so there were concerns about what this would mean. It was very controversial and everybody had their own sort of little predication. We often would, when asked, say well we think it could eventually reach 20 or 30% but there are going to be some people always who probably aren't going to be capable of self-therapy and don't have anybody to help them. I used to say, well you know I like to think of it this way – If you look at the typical chronic dialysis candidate maybe half of them are too frail to do self-therapy, too frail, maybe their mental facilities aren't enough that they could learn and this kind of thing. So if you say, okay, half of the patients are eligible candidates and of that half maybe half of those would say, yes, I'd like to do that, and the other half might say, no I want somebody to take care of me in a unit or I want to use a machine, I don't want to do that. So I would often say, I think half of half, 25%. That was my…

DWM: Pretty good.

KN: But we were all just guessing and we did get fairly close to that when it was at its peak.

DWM: Right. Talk to me about the evolution of catheters and how you all came about finding and developing the Missouri swan neck catheter.

KN: Well when you talk to Dr. Twardowski you'll get the full story. He has spent a lot of his life thinking about ways to improve dialysis and in addition to conceiving the hollow fiber dialyzer that you'll talk to him about, he's always I think thought about peritoneal catheters. So when he came here he was very interested in what would be the best design. It was his idea to develop the swan neck because of the evidence in the literature that if the exit site points down, points caudally, that it will drain better, it will be less predisposed to infection and he did surveys of our own experience showing that when it was pointed downward exit site infections were less than when it was up. The idea that an upward pointing exit site collects sweat and debris and is more prone to problems seemed reasonable. Then as it enters the peritoneal cavity it should also point downward because many of these catheter materials have a plastic memory and if it's not pointing downward when it goes into the peritoneal cavity and you have it pointing sideways and then bend it down it's constantly going to try to straighten itself out so you're not going to keep it in the lower abdominal cavity very well. So the swan neck or the U-shaped bend helps to have the catheter want to assume a natural position where things are pointing down. Then he developed his special little hat that goes into the entry area there and so this worked very well then he studied it and it's become very popular. One of the biggest advances from our point of view and worldwide that's catching on more and more is the presternal catheter that he developed.

DWM: Yeah. Yeah.

KN: And the idea there was that the abdominal folds and some people have a lot of fat folds and exit sites get hidden in under there, they're hard to keep clean. They can't get into bathtubs. He said if it came out here then this is a lot less mobile. There's not going to be nearly as much jerking and pulling on the catheter and its exit site. It can be much more readily cleaned. They can sit in a bathtub with their exit site up here. So he developed that and we've had wonderful luck with that presternal. They're now using that almost exclusively. Many centers are going to the presternal more and more. I presented the concept of the presternal catheter back in the early days at a meeting in Italy and so it was a funny thing because on my slide I was listing all the advantages and one of them; 1, 2, 3, 4, 5 was that it's great for bathtub lovers. Well the Italians, all of a sudden, they got very interested. Woo, you know. And I think they thought I meant something different from people who loved to take a bath.

DWM: The American culture meets the Italian culture.

KN: Yeah. I'll always remember that. I think I might have changed the slide or explained it in future talks; now by here I mean people who love to take a bath.

DWM: That was very funny.

KN: Yeah.

DWM: You know there's been a lot of discussion about hemodialysis and the fact that as chronic units became more available, we changed from the Scribner thought which was that you wanted to get people on dialysis but then you wanted them to go home and do home therapy and that as centers sprang up less people went home. Training, I mean deciding who can go and then training people is quite an endeavor. It's very labor intensive. You all have done a lot with training over time. You have been very committed to home training. Has that philosophically been your thought that people ought to try to go home?

KN: Yes, very much so and we've worked very hard to get people home. We think there are many advantages and CAPD really helped to get people back in the homes. Nowadays with the daily home hemo and so on I think there's a big shift to get more and more people on home hemodialysis as well. But for a while there, you know, home hemodialysis had dwindled down to almost nothing. It seemed to require too much training, a six-week training period, always questions about how many people could do it and how much work it was. The new daily home hemodialysis machines are being designed to make it easier for the patients to do that and Dr. Twardowski, that you'll be speaking with also, designed probably the very first daily home hemodialysis machine that presumably the goal is to have it be an almost one button technology sort of thing. But CAPD really leant itself to that and we've had wonderful nursing staff to do the training. We've had Ann Campbell, a patient educator, who has been with us for years and years and years and she does such a marvelous job in helping patients select a therapy, giving a course on what we have to offer and we feel it's a great strength of our program and any program if they can offer a patient many, many options and then talk with that patient about the advantages and disadvantages of each and then focus on that patient and their lifestyle and their characteristics and help them decide what would be the best fit for them right now. Then to have the program be ready to quickly make a change if the patient's lifestyle changes, the patient's health changes and say this therapy isn't the best for you right now, maybe it's time to switch to this. So one of our goals has always been to offer as many options as we can and to have a real quick trigger to move patients from one to the other just to try and match them up with what seems best for them and always have the patient play a huge role in deciding what is best for them. We shouldn't make that decision and say this is what's best for you. We've been involved in many studies that have looked at this around the country and many other centers have done these studies too and they find that many centers do not educate their patients about all the options. They do not offer them all the options. They just shove them into one simple option because that's what they offer and so we think a great strength that we've had is to have a whole menu that we can offer and help patients choose at the beginning and as each week goes by choose a different menu if they want to do that.

DWM: When you started that early hemodialysis in the temporary dorm behind the hospital…

KN: Yes.

DWM: with Dr. Van Stone, did that grow pretty quickly from 1974 _____?

KN: It did. I think it wasn't long until we were getting up 20 or 30 patients or so on chronic hemodialysis. The Missouri Kidney Program has been a very helpful agency in the state of Missouri helping to fill in the gaps where we might not have Medicare covering things and so on and it helped to make it very easy to expand our programs. We found patient funding so that we could pretty much open the doors and take all comers. Then, in addition to the National Kidney Foundation, there's a local Columbia group. Ann Campbell, that I mentioned, she is, I think, the treasurer now but that's been here for many, many years and they raise a lot of money locally to help fill in the gaps. So all of these things opened up not only when Medicare came along but then with the support of Kidney Foundations and the local Columbia group and the Missouri Kidney Program. The Missouri Kidney Program, which was state funded, provided not only patient care help but also research money as well.

DWM: Hmm.

KN: To do dialysis-related research.

DWM: That is very generous. There are certainly many places that, even after the passage of the law in 1972, had big issues with patient funding.

KN: Right. Oh yes, yes. So we were blessed very early on to be able to grow. Then they eventually closed down the temporary building and moved into a really nice modern facility and it was in collaboration with DCI. The school here was very comfortable with DCI because they're a non-profit corporation.

DWM: Right.

KN: They mainly work with medical schools. And we're now in another different new facility that's out near the Marriott where you stayed.

DWM: Right.

KN: Beautiful outpatient dialysis facilities now in collaboration with DCI.

DWM: Yeah. I know Dr. Teschan has been very involved also in DCI.

KN: Yes.

DWM: And John Sadler.

KN: Right. Right.

DWM: They've had a very clear mission about their outpatient dialysis for many years.

KN: Oh yes, yes. Well I had the opportunity to work with the colonel at Walter Reed and so we've had a good relationship ever since. We honored him one year. You know each year at our Annual Dialysis Conference we try and pick out someone that we feel has made big contributions to the hemodialysis field and someone who's made big contributions to the peritoneal dialysis field and he was one of our hemodialysis award winners one year. It always gives me a pleasure to have some of these old friends come in and receive the recognition that they deserve.

DWM: Right. Tell me how the annual dialysis meeting began again. What year was your first meeting?

KN: Oh that's a very interesting story I think. One of the offsprings of the NIH contract that we had with Moncrief and Popovich to collaborate in studying CAPD was the desire the NIH had to develop a registry, a CAPD Registry. So these contracts that we had with NIH were expanded to become the CAPD Registry. So we ran the CAPD Registry from '81 to '88. Now in the early years Austin Diagnostic Clinic – University of Texas, they were the data coordinating centers and we, the University of Missouri, were the clinical coordinating center. Then eventually when the contract came up for renewal we continued to be the clinical coordinating center but the data coordinating center went to the Emmes Corporation. So each year we'd publish an annual report and by the time we were done we had a large number of centers participating. I think it's right here in the front; we had 485 clinical centers participating and 25,000 CAPD patients.

DWM: Wow.

KN: So we were collecting data on those patients continuously and we published the annual report from 1981 to 1988. Now around that same time, '81, the folks at NIH approached me and I think Nancy Cummings was one of them, she was in charge by that time, and said you know it would be nice if you would call all of these centers together for a meeting and talk about experiences and help other centers that are just getting started to gain some insights from what you've been doing and what others are doing and maybe you could even invite centers who are not yet involved in the registry but who are thinking of starting CAPD and suggest they come to the meeting and maybe learn how to do CAPD and maybe this would help them about their decision to get started and help them know. I said, this sounds like a wonderful idea. My impression was in that conversation that NIH was going to fund this meeting and add that on to the contract. So I started making some calls about possible places to have it, thinking of a convention center. I remember looking into St. Louis and that sort of

thing and I was well underway when I was talking and she said, well now let me make it clear that we don't have any funds for this. Oh. And she said, I guess the best way is to just charge a registration fee to cover the expenses. But we'd like you to go ahead and do that, so we did. So we organized the first one in 1981 in Kansas City. I think there were less than 500 people but it went very, very well. At that time it was just a CAPD Conference. The first one was just called the CAPD Conference.

DWM: That's right. I remember.

KN: Then it was so well received and we were able to cover the expenses for the invited speakers and the CME people here then organized it and they did a wonderful job with the nutrition breaks and sit down lunches, things like this. So people loved the meeting. So we said we'll just do it every year and it grew and it grew and it grew and now this year in Houston will be the 29th. So I've had the privilege and the chore, I guess also, of being the Program Chair for now the 29th year. We're now working on the 30th already as well. But it grew and peak attendance was over 3,000. After 9/11, oh, 2,500 to 3,000. It's interesting with the economy where it is now and many centers not allowing their people to travel, we're still doing quite well with our registration. I think we'll go over 2,000, which is quite good under the circumstances for the Houston meeting. But it grew and grew and then we changed the name. We went from CAPD to the Peritoneal Dialysis Conference and then the pediatricians wanted to join so we had the Pediatric Dialysis Symposium along with it. Then we added hemodialysis so eventually it became the Annual Dialysis Conference.

DWM: Right.

KN: Yeah.

DWM: As I recall too it has a fairly good international, ah, flare.

KN: It does. We have probably almost a third of the attendees are from outside the United States and usually we get abstracts from 40 to 50 countries and the registrants are, I think typically in the last few years, from 60 countries so we have just about every country represented.

DWM: Yeah.

KN: We've never had anybody from Antarctica but just about everywhere else.

DWM: Also, I think you've been fairly involved in the International Society for Peritoneal Dialysis. Is that true?

KN: Yes. Yes. And this sort of got its start way back in… I think Alexander _____ from Mexico, came and I think he visited my office and he was very interested in having an international meeting on peritoneal dialysis in Chapala, Mexico. So I said that sounds like a great idea. He asked my help to help him organize this so this was held June 26, 1978. That's Dr. Oreopoulos and me up there. I won't go through all the names but many of the names we've been talking about are right here. But it was a very nice meeting and it was 1978 so for many of these people it was their first time to hear about CAPD. They talked about CAPD and what it might mean. I think I even had some things to say about CAPD to the group. Bob Lindsay from Canada; I think this was where he showed his famous line of Moses carrying the tablet but on it, it said CAPD. He named Moncrief and Popovich as the modern day equivalents of Moses bringing the tablet down from the mountain. But this meeting went very well and there was a tremendous excitement about CAPD and what this might do for PD. At that meeting they decided that maybe we should do this every three years. The group from West Berlin, _____ and Professor _____ agreed that they would host the next one in 1981. There was a discussion about whether to form a society and at that time they decided, no let's just have a meeting, no society. So I was appointed as sort of the executive secretary of the group and it was my job to help the group in Berlin organize this 1981 conference. So I flew over there once and had a great opportunity to interact with them. Then this meeting went very, very well and it was decided to have another meeting in 1984 and I think that was the Washington meeting…is that where that…because, yes, by this time, I'm thinking in 1984 Jack Marr would have been up in Connecticut but Jim Winchester and I can't recall where Jack was but Jack Marr played a major part. But I think it was at that meeting that it was decided… Maybe he was back at the Armed Forces. That's why it was. Jack had now gone back to Washington. He was at the Armed Forces School of Medicine. You know he went to Georgetown, Missouri, Connecticut. He was back in Washington. So he and Jim Winchester, who was still at Georgetown, agreed to host this one and then they decided, I believe, that a society should be created.

DWM: Um hmm.

KN: So I think it was at that meeting that the society was created and Jack Maher was now elected at the first president. I think I have the dates right. So it took a while but then it became a society. Dr. Oreopoulos was publishing what was called the *Peritoneal Dialysis Bulletin* in those days.

DWM: Um hmm. Yep.

KN: And it wasn't long after that that there was a great interest in the society taking over that journal and so I arranged a meeting with Jack Maher and Dimitri and I think we met in Washington. We discussed having that journal become the official journal of this new society. So the meeting went very well and Dimitri agreed to stay on as editor for a number of years. The name was changed to the Peritoneal…I'm blocking on it now.

DWM: The Journal of …

KN: *Peritoneal Dialysis International*, PDI.

DWM: That's it. PDI.

KN: I was doing ISP and PDI. But it's *Peritoneal Dialysis International*.

DWM: Yep.

KN: I should have known that. But yeah, the Third International Symposium was held in Washington, 1984, then ISPD was established. There were 28 founding members and Jack Maher did a lot of the work in creating the constitution and all of that sort of thing. Then it was in 1983, I think, that Dimitrios turned over the *Peritoneal Dialysis Bulletin* to the society and remained as editor.

DWM: Okay.

KN: So a lot of that interesting all started with Alexander Trevino in Mexico, then off to Berlin as an informal gathering and then becoming an official society at the meeting in Washington.

DWM: Washington in '84. Were you also involved with ASAIO and ASN during this time?

KN: Yes I was President of ASAIO.

DWM: Oh, I didn't realize that.

KN: And let's see, woo, what year was that? I'd have to get my CV out to be sure but I did a lot of my early research presenting at the ASAIO meetings. It was a godsend for somebody doing peritoneal dialysis. So a lot of my early peritoneal dialysis research was accepted there and presented there and then I published it in the Transactions of ASAIO. Then I was eventually appointed to the Council and worked my way up and so I became President of ASAIO. It was a lot of fun. That society has changed a lot, you know, it's not dominated by nephrology like it used to be. Cardiovascular surgeons and so on have a major role in ASAIO. But in the early days it was mainly a gathering place for the dialysis people.

DWM: Yeah.

KN: And a lot of the early ideas were shared there. Moncrief and Popovich had their abstract rejected but eventually they were invited back to present many talks and developments on CAPD.

DWM: Why was ASAIO a godsend? I mean were you just not getting a real forum in other places and they offered you a forum?

KN: I think again that the American Society of Nephrology, which was also in its infancy, and I went to the very first meeting of ASN. I remember I think it was L.A., California. I remember being there with the colonel. I was at Walter Reed; I think I was still Walter Reed. But it was, I think, focusing a lot on renal physiology and micropuncture and clinical nephrology but they weren't quite sure how much interest there might be in dialysis. Although it's interesting, I submitted dialysis abstracts to ASN even at the early days, I think even at that first meeting. I think I might have had one of the few, if not the first, abstracts ever accepted at ASN in the dialysis field. But ASAIO founded by George Schreiner and others who felt there was a need for a place where the people could talk about dialysis and its developments and share ideas and focus on that. So it was a wonderful forum for sharing early ideas in the dialysis field. I enjoyed it very much.

DWM: It sounds like it was a gathering place for people like Belding Scribner and…

KN: Oh it was. You got to meet all of these wonderful big names and interact with them and have them get up and comment on your research and what you were saying and this sort of thing. Even there peritoneal dialysis was sort of out in left field. The main focus was on hemodialysis so the fact they would let some peritoneal dialysis papers in the door. I think Jack Maher may have defended me to some of the big names in the early days saying, you know well peritoneal dialysis is dialysis too but there's no machine involved. In those days there didn't happen to be a machine. But they let me in the door and I presented many of the peritoneal dialysis papers there. One of the most important, I think, was we followed up our work on peritoneal sodium sieving with some studies looking at solutions with different sodium concentrations and we progressively lowered these concentrations. It was a company other than Baxter that was making solutions in those early days that made them for me and I had 140, 130, 120, 110, 100. I showed that you could now, by having that very steep concentration gradient for diffusion, have sodium keep up by diffusion added to the convection and you could remove a balanced sodium and water ultrafiltrate that looked like ECF and I found that, at least with these very hypertonic exchanges 7%, you had go to down to a dialysis solution sodium 110 to 100 to get balanced removal of sodium with your UF. So then we published a number of diagrams to explain well what is going on here, what are the pathways being used. It was in that paper that we proposed that there might be a selective path for water transport across cells though which electrolytes couldn't follow so indeed we conceived of the concept of a transcellular water pore as an explanation for what we were seeing. We suggested that the diffusion might take place through intercellular gaps, not through the cells, and that some of the UF might be coming through intercellular gaps as well so that if you just did UF and had no concentration gradient you got a mixture of the intercellular gap ultrafiltrate that looked like ECF fluid plus pure water and it mixed up and you had more water removal than sodium and

you had the sieving. But if you now had a steep concentration gradient then sodium would be coming through the intercellular gaps in great speeds along that gradient and you could help to fill up the free water by all of that extra sodium coming through and we proposed that. So I take great pride in that paper because I think it was one of the early suggestions that there might be transcellular water pathways.

DWM: About what year would that have been that you described that?

KN: That would have been like 1970, early 70s I think.

DWM: Wow.

KN: Yeah.

DWM: Yeah.

KN: Maybe '72, around in there.

DWM: Do you remember some of these early people? Can you tell me about them, like Fred Boen and Henry Tenckhoff?

KN: Yes. Henry Tenckhoff and Fred Boen. I was invited to Seattle to speak on CAPD several times and one time I was invited to be a major speaker at, I think, it was the 25th year celebration of the chronic hemodialysis program in Seattle. They invited me to speak and there were a lot of receptions. I think we went to Dr. Eschbach's home for one of the receptions and I was chatting with Henry Tenckhoff. He and Fred Boen had been very much involved in their intermittent peritoneal dialysis program with Henry working on catheters and Fred Boen working on all the logistics and so on. I asked Henry I said, what do you feel about CAPD and the idea of CAPD after all of your years with IPD, intermittent peritoneal dialysis? What is your reaction to CAPD? He said, I wished I had thought of it. Which I thought was a very, very generous statement to make from somebody who wasn't, you know, envious or so on. He said, I wished I had thought of it. But he was a very interesting fellow. We have invited Henry Tenckhoff for an award, I think several times, and he won't come for awards. So one year we showed his picture and said how much we were appreciative of all he had done. But he is very reluctant to go anywhere and accept an award. We did get Fred Boen to come and present one of the awards for outstanding achievement. I met Fred many times. He was back in the Netherlands pretty much after I started my career. I had read his book and so it was wonderful to meet him in the Netherlands. I went to his hospital several times. They invited me there for some big celebration of their hospital's anniversary; I forget which one it was, of their dialysis program so I went there and gave several talks and interacted with them. But he was always a very friendly, happy man and he'd done a lot of very important pioneering work.

DWM: Yeah. Did you know Dr. Scribner very well?

KN: I knew Belding very well and was out there when they honored him, as I mentioned, and then he used to interact with me in many ways. I served on a committee with Belding Scribner and Lee Henderson. There was a book that was organized by Dick Tannen and it was called *A Quarter Century of Nephrology: Commemorating the American Society of Nephrology's 25th Anniversary*. Belding Scribner and Lee Henderson and I were the subcommittee to write about dialysis in here.

DWM: Hmm.

KN: And so we… Somebody from ASN put together all of the abstracts on dialysis that had been submitted to ASN over the 25 years and we were then to write a chapter reviewing these highlights and what we thought were the most important, the biggest advances, and this kind of thing. We talked about all kinds of things. We talked about the Moncrief and Popovich original abstract rejected by ASAIO but eventually ASN did accept one, you know, so all kinds of things like that. I worked very closely with Belding and Lee on that chapter. Dick Tannen, I think who was the overall organizer; I think he was President of ASN at the time, he called this… Richard Tannen, President 1992. He called this whole committee the gray-haired committee. This is the picture of the group right there. So I got to work with him there. I saw him many times at meetings. He would often call me urging me to write something about that he was very interested in controlling volume in his later years. He just felt that sodium and water removal and adequate control of volume was being neglected and how important this was and that people were leaving patients volume overloaded and filling them up with antihypertensives when they should be controlling their volume first. He would call and urge me to do something about this and write an editorial or one of his colleagues would be going to present this and he'd hope that I would meet with him and tell them how important this was and this and that sort of thing. He'd often say, you know you're younger than I am and I won't be around as long as you and it's up to young guys like you to carry the torch of what's important in dialysis. He'd often charge me with the need to carry on once he was gone.

DWM: Hmm.

KN: So I had many great… His wife was wonderful. She would often be at meetings and so Mrs. Scribner and my wife and our children would often go off and do things together. I think when we were out there Chris Blagg and his family were very hospitable too. I think one time we went to some reception and we left our kids with the Blagg's babysitter at the Blagg's house. So I've had a lot of interactions with that group.

DWM: With the Seattle crowd.

KN: Yes.

DWM: Tell me about Lee Henderson.

KN: Well Lee Henderson was a young faculty member when I arrived as a fellow and at that time he was very interested in vitamin D and very interested in peritoneal dialysis and peritoneal transport. He was working very closely with _____ .

DWM: Um hmm.

KN: On this idea of hemofiltration and developing a hemofiltration membrane. That was a big thrust while I was there. So Lee and I then would work together. He was the attending many times when I was on the consult service as a fellow. Back in those days the fellows were much more independent than they can be now so the fellows often saw consultations and wrote recommendations and would briefly mention them to the attending but on rounds with the attending you'd often pick one or two that you'd go over with in detail. So it was much different. Marty Goldberg was the head of nephrology. Russ Elkington had just stepped down. Russ Elkington had been editor of the Annals for years, a big acid-base man. He brought the first flame photometer to Philadelphia.

DWM: Yeah.

KN: And made his name because he could measure sodium with the flame photometer. Marty Goldberg had just taken over and Lee Henderson was a young faculty member. Lee was a wonderful clinician. He had been trained at Peter Bent Brigham with Merrill and had come down to Penn from his training with John Merrill and he instilled a lot of good clinical knowledge both into my brain and that of Jay Puschett. And it was a pleasure to work with him. Then through the years I've kept in close touch with him. Then he eventually went out to the Scripps Clinic for a while and then he joined Baxter. He was one of their Vice Presidents for Research.

DWM: Right.

KN: So when he was Vice President for Research at Baxter he played a major role in providing some Baxter funds to support some of our peritoneal dialysis research and so we interacted with him in that capacity.

DWM: And also it sounds like Oreopoulos, you and Dr. Oreopoulos, have been friends a long time.

KN: Yes we have indeed and we have just spent a lot of time together at meetings. When I retired Dr. Oreopoulos was one that flew down for the retirement reception, Lee Henderson was here so a lot of these people took the time to fly down for my retirement party. Now Dr.

Oreopoulos and I keep in touch almost on a daily basis. He sends me emails. He loves to find interesting philosophical things in the Internet and send them out to his friends so we take turns sending back and forth these things. He's quite interested in theology, philosophy and as a young man I think he went to school in a monastery and was educated by monks. He almost became a monk in the Greek Orthodox tradition. From time to time he takes a month off in the summer time and goes to this monastery where he lives in isolation with the monks. It's that monastery where no females of any kind are allowed. They don't even allow cows in the pastures there. But he goes there and he thinks. A very interesting man.

DWM: Yeah.

KN: A very deep thinker.

DWM: What do you think is the future for peritoneal dialysis? What do you see in the next 10 to 20 years for peritoneal dialysis?

KN: Well I think that it has a very important role to play in the lives of some patients and I think it's a wonderful starting therapy for many patients. I think that, you know, I've been an advocate of avoiding starting dialysis late when patients are already showing the ravages of uncontrolled uremia and so on and I've often said peritoneal dialysis can be started and help to control fluid balance, acid-base, electrolytes, BUN, creatinine and you can start it fairly early at even one exchange a day and build up to two and three and four. John Burkhart and I used to talk a lot and write about incremental dialysis with PD.

DWM: Early start.

KN: Early start and use it and very little of this has been done. There are a lot of arguments as to whether it really does offer any long-term survival advantages and that sort of thing. But it's something you can do without using your blood access sites right away and so on and many people, whenever you start them, could stay on peritoneal dialysis for a number of years and maybe some, as their residual renal function declines, are going to need to switch. But I'm a true believer that many, even big people, can be carried if you increase the volume of exchanges and so on. Peritonitis rates have plummeted down to very low levels compared to what they used to be and that may even get better in the future. We need more biocompatible solutions. Peritoneal fibrosis and encapsulating peritoneal sclerosis, you know fortunately it's not that high in incidence. But I think solutions can be developed where that's less likely to happen, that that could become a very rare event also. So I think once we have optimal solutions that there is a tremendous role for at least first line of therapy in many, many patients and I think the lifestyle advantages of the freedom, the independence, the steady state chemistries, saving the exit sites, the blood access exit sites, that it should be utilized more. Most nephrologists, when polled, say it's underutilized; most everybody agrees. Well why is it underutilized? Well because so many programs now aren't training young nephrologists to do

peritoneal dialysis and many programs don't have adequate peritoneal dialysis programs which baffles me because it's suppose to be a required component of accreditation and if you don't have enough hemodialysis patients you're in trouble, if your fellows aren't seeing enough transplant patients you're in trouble and yet they accredit these programs where the fellows are seeing sometimes almost no peritoneal dialysis patients or they may farm them out to some other hospital that has a few peritoneal dialysis patients and say, see we've fulfilled the requirement. So a lot of young nephrologists are coming out and they're not comfortable with it, they don't know much about it, they can't really add it to the diversified menu of their programs because they've not been trained properly and they don't know. So you have all of these programs, these units, that are hemodialysis oriented and nothing else. So what do they do? They don't tell the patients about peritoneal dialysis. They just tell them about what they have.

DWM: Right.

KN: So I think, in my opinion, that's a lesser program. I think that a good program can talk with patients about the options, not push any kind of dialysis on any patient but to think it through considering the patient's desires and what's best for the patient, talk it over and so on. I think peritoneal dialysis could be utilized a lot more than it is. I think as a starting therapy that, gosh you know, it could easily be used in 25 or 30% or more. Just like I said before. Now there are survival advantages to peritoneal dialysis in the first couple of years. Over and over again the USRDS, a recent paper from New Zealand, they all keep showing that. Now after the first couple of years then there seems to be survival advantages for hemodialysis especially in the older and the groups with comorbidities. If you look at the younger healthier dialysis people waiting for a transplant there may continue to be PD survival advantages for them. But if you lump it all together the survivals over a long period of time like the recent USRDS lines are really very similar. So should you make the decision based on survival alone? Well I think there are many things that are also important in thinking about the choice other than maybe percentage differences in survivals that are based on huge population studies like lifestyle…

DWM: Right.

KN: and whether you work or not and what your family situation is and whether you're an independent person, whether you want to be taken care of by dialysis personnel. I've often said that I think that daily home hemo is a nice child of CAPD and intermittent hemo. It kind of incorporates the advantages of both. It's more steady state, it's more nearly continuous, it's home; it has those features of PD and it has the blood access without people having to worry about peritonitis and solution chemistries and peritoneal damage and running the stuff in and out of their abdominal cavity. So I think that the future is going to be big for daily home hemo. I've often said, wouldn't it be wonderful if you actually had your daily home hemodialysis machine able to make peritoneal dialysis solutions so people could go home on that machine

and do peritoneal dialysis until they're ready to switch and then switch over with the same machine to daily home hemo.

DWM: Ah.

KN: You know these machines make; the Twardowski machine, beautiful sterile solution that could be used to do PD exchanges and a machine could easily be designed to actually do the CAPD exchanges for a person, step up to it and have the exchange done and do PD for a while and then use the same machine and modify it to push a different button and use it for your daily home hemo. I've thought, wow, wouldn't that be a nice way to pluck the advantages of early CAPD and then eventually going to daily home hemo.

DWM: Yeah. That makes perfect sense.

KN: Yes.

DWM: When I was looking at a few things for you I came across an article in *Nova News Now*, which I gather is a little newspaper maybe where you and Georgia summer in Nova Scotia.

KN: Oh yes.

DWM: The comment the author made was that when he or she, I guess, maybe looked at your resume that it was mind-boggling all that you had done and I would certainly agree with that. But they mention in that article your music; that you are a musician.

KN: Oh yes we are, Georgia and I. We love music. I play the trumpet and she plays the piano, organ, clarinet and saxophone. We've been summering in Nova Scotia since 1999. I can still work on the Annual Dialysis Conference wherever I am because I do a lot of it on my daily email.

DWM: Right.

KN: Inviting the speakers and corresponding with the speakers and all of that. But up there we are in two community bands. We're in one in Liverpool, Nova Scotia, the Mersey Band. We're in the Bridgewater Fireman's Band. We play trumpet and piano duets at the church services in Liverpool. Georgia sometimes fills in for the organist. Then often other musicians join us. I'm also in a brass group called the Privateer Brass. So when we're up there during the summer we have a parade, a concert or some kind of rehearsal almost every day all summer long. They're big on parades and they love to have their concerts and the bandstands next to the ocean in the evenings in all of these little towns so we travel all over with the bands. Some days we have two parades with two different bands in two different towns and so we get stretched.

DWM: I'm glad you've just gone up there to relax for the summer, good plan.

KN: Yes but we really enjoy it. They welcome us with open arms and we've become important parts of these musical organizations and now this summer Georgia's also been invited to join a wind ensemble so she'll probably be in that. There's a big band up in Mahone Bay and we've been invited to join that but that conflicts with the rehearsal for… so we're almost signed up for more than we can do because of the conflicting parades, concerts and rehearsals but we do the best we can and we really enjoy it.

DWM: That's wonderful.

KN: Yes.

DWM: Is there anything else you think we ought to talk about today before _____?

KN: Well you've asked a lot of good questions. I've enjoyed sharing all this history and all these memories with you. I think you've covered a great, great deal of my life.

DWM: Well I greatly appreciate your time.

KN: Well thank you again for letting me do it. I'm very honored to be interviewed with all of these other big name figures that you are interviewing.

DWM: You are definitely among them, no question.

KN: It's a great honor to be included in such a group.

DWM: I may talk to you about some of these pictures. I want to make sure I make a note of…I didn't realize you had a little article that you had written here so I want to…

KN: This is the one I emailed you about that's my _____.

DWM: If you emailed me I missed it somehow because I have not…

DWM: So this is a story from your memoirs _____.

KN: When Bob Longnecker sent his patient out here I got a call from a New York newspaper. I don't remember whether it was *New York Times* or what. They said they were very interested in this New York patient coming out for this therapy and could I tell them the name of a center in New York that was providing CAPD, they'd like to just go and do a story on it. I said, there are no centers in New York. Well where are the centers? I said, well just in Missouri and Texas

right now. And this reporter said, are you trying to tell me there's something in Missouri that's not in New York? I said, well that's exactly right. So I thought that was funny. *Time* magazine came out. They wanted to do a story on CAPD and so they came and interviewed me, took some pictures and this is the *Time* magazine drawing right there. So they did that and they did it very, very well but I point out in here that the story on CAPD was on page 82 of that particular issue of *Time* magazine and on page 85 there was a story and picture of a very exposed Farrah Fawcett-Majors and I said never before or since has a CAPD article been up against such competition. So that was funny. The other one that I enjoyed was Medicare was working on how to reimburse for CAPD.

DWM: Right.

KN: And they were trying to learn about it and so it was about a year after we got approval for the bags. They asked if they could come out from Baltimore and meet with me and talk about this technique so they could get some ideas as to how to reimburse it because they agreed it should be covered. They happened to fly into Columbia into the local airport on a rainy, rainy stormy night and the plane landed on the runway and went off the end of the runway and into the mud. It just sunk in the mud right down to the belly of the plane. The landing gear was in the mud. The stewardess, without batting an eye, threw down the steps and said, here we are. And so all of these folks, there must have been at least half a dozen of them, came down the ramp and stepped into the mud and sunk up to their knees. They sloshed through this mud to the terminal and ended up at their hotel and the next morning when I went to meet with them their pants were all muddy up to the knees. We had a good meeting but at the end of the meeting they said, Dr. Nolph if we need to discuss this with you any more would you mind coming to Baltimore. I thought that was a great story.

DWM: That may be the last time the U.S. government actually came out to Missouri.

KN: They didn't come back. Well I better introduce you to Zbylut then.

DWM: Very good. Okay.

END OF DICTATION

Dugan W. Maddux, MD
DWM/dlb
T: 04/19/09