Distinguished Conversations

Once again, *Kidney News* brings together two outstanding clinicians, scientists, teachers, and leaders in nephrology and medicine in a "Distinguished Conversation." Each has transformed the practice of nephrology with excellent examples of bed-to-bench problem-solving, bringing innovative care back to their own as well as to our patients.

Joel Kopple, MD, is currently Professor at the David Geffen UCLA School of Medicine and the UCLA Fielding School of Public Health. He served from 1981 to 2007 as Chief of the Division of Nephrology at Harbor-UCLA Medical Center. Known as the father of renal nutrition, Dr. Kopple has contributed greatly to our understanding of the impact of kidney disease on nutritional status and on the influence of nutrition on kidney function and health. Toward this end, he has published more than 500 papers, books, and chapters, including the authoritative "Nutritional Management of Renal Disease." He has garnered many prestigious awards, including the National Kidney Foundation (NKF) David M. Hume Memorial Award, the ASN Belding H. Scribner Award, and the Louis Pasteur Award of the University of Strasbourg, France.

Dr. Kopple served as President of NKF and the International Federation of Kidney Foundations. He played a seminal role in founding the International Society for Renal Nutrition and Metabolism, the International Federation of Kidney Foundations, and World Kidney Day, and he served a central role in founding the Rhoads Research Foundation of ASPEN and the National Kidney Disease Education Program (NKDEP) of the National Institutes of Health. The NKF Council on Renal Nutrition established the annual Joel D. Kopple Lectureship and Award in his honor, and the International Federation of Kidney Foundations also established an annual Joel D. Kopple Award.

Richard Glassock, MD, is Professor Emeritus at the David Geffen School of Medicine, UCLA. He is an internationally known expert in nephrology, especially glomerular disease, the aging kidney, and kidney function.

A native Californian, Dr. Glassock attended Duke University School of Medicine, graduated from UCLA Medical School, and trained in nephrology at the Brigham and Women's Hospital and in immunopathology at the Scripps Research Institute. He has held innumerable leadership positions, including Chair of Medicine at UCLA Harbor Hospital and at the University of Kentucky School of Medicine. He also served as Chairman of the American Board of Internal Medicine, President of NKF, President of ASN, and founding Editor-in-Chief of ASN NephSAP. Among his many honors are the NKF David M. Hume Memorial Award, the UCLA School of Medicine Distinguished Achievement Award, the NKF Distinguished Service and President's Award, the American Kidney Fund Torchbearer Award, the Medal of Excellence of the American Association of Kidney Patients, and the ASN Robert G. Narins Award for educational excellence. He has published over 600 papers, books, book chapters, and monographs. He continues to actively teach internationally and is widely sought for his academic and clinical insights.

Please enjoy this discussion and let us know what you think of the series.

Richard Lafayette, MD, editor-in-chief, ASN Kidney News

Joel Kopple, MD

Richard Glassock, MD

Dr. Kopple: Why did you become a nephrologist? Were there other fields you considered as alternatives?

Dr. Glassock: Thank you, and the ASN, for this opportunity to tell you how proud I am to be part of the discipline of nephrology, especially since I believe it has done so much to provide relief from suffering and extend lives over the past 50 or 60 years. I hope I've been able to do a few things to help nephrology move along during my career.

I did not immediately start out to be a nephrologist, and I had very few role models to help steer me careerwise, other than a primary care physician during my high school days. I also didn't have any doctors in my family, so my initial exposure to nephrology was a chance event—a little bit of serendipity and good luck.

During my first year of residency at UCLA in 1960, patients were assigned to residents on a rotational basis, and a 17-year-old girl with end stage renal disease (ESRD) came under my care. I never knew exactly what she had, but in retrospect, her symptoms were certainly suggestive of some form of hereditary disease, perhaps medullary cystic disease. Her physician of record was Morton Maxwell, who had just joined the Department of Medicine at UCLA as a young faculty member doing clinical nephrology (although the term "nephrology" wasn't widespread at the time) and was trained by Homer Smith. It became apparent there wasn't anything we could do for the patient other than intermittent peritoneal dialysis, so it was decided that maybe she would be a good candidate for a kidney transplant. Transplantation of kidneys from related and unrelated persons had started in Boston under Murray and Merrill and colleagues in the '50s and early '60s, but was not yet a procedure that was widely applied to treatment of ESRD.

After being tissue-typed using leuko-agglutinin techniques, she received a kidney from her mother in the late fall of 1960. It turned out that they were reasonably compatible on the basis of leukocyte antigens. She was treated with cyclophosphamide, actinomycin, and steroids, as azathioprine was still an experimental drug at that time.

The surgery itself was reasonably successful, although she did develop a ureteral leak. Two weeks after transplant, she experienced a severe rejection, which was surprisingly reversed by high-dose steroids. To my knowledge, it was the first time an acute allograft rejection had ever actually been reversed by a drug. However, due to multiple rejection episodes, eventually she succumbed to the usual complications of excessive immunosuppression, probably a cytomegalovirus pneumonia.

The case transformed my professional career. I became very interested in and committed to pursuing nephrology, specifically transplantation. I participated in the care of several additional cases of renal transplantation at UCLA. Fortunately, the urologist leading the renal transplantation effort at UCLA, Willard Goodwin, happened to know Joseph Murray and John Merrill at the Peter Bent Brigham Hospital in Boston (Now Brigham and Women's Hospital; BWH) very well, and with a telephone call, he managed to get me a fellowship position in Merrill's lab, which I started in July 1963.

My co-fellow at the time was Bernie Carpenter. Bernie has unfortunately since passed away, but he and I were the first two medical transplant fellows at BWH, and our careers were intertwined for many years subsequently. Bernie was a great

friend who made numerous seminal contributions to the field of Transplantation, and remained at BWH for his entire professional career.

The BWH experience from 1963 to 1965 solidified my career choice. Under the influence of John Merrill, George Thorn, Joseph Murray, and Gustav Dammi (the Chairman of Pathology), my career took another twist when I was asked to go to Scripps Clinic and Research Foundation and undertake training in immunopathology, under Frank Dixon, and bring it back to the BWH. At the same time, Bernie Carpenter was sent away to develop a transplantation immunology expertise and would return a few years later.

This "outsourcing" was a common approach in those days: taking ambitious young fellows, encouraging them to pursue a career, giving them an opportunity for outstanding training in a basic laboratory of international reputation, and then having them return to the institution with a commitment to develop a program. I fell into that mold almost serendipitously, but it had a profound effect on my future. By the time I finished my year-and-a-half training with Frank Dixon in La Jolla, I was well on my way to a lifelong commitment to immunology, glomerulonephritis, transplantation, and clinical nephrology. That is really how my nephrology career began.

Dr. Kopple: I became a nephrologist several years after you, and I remember that during the treatment of people undergoing chronic dialysis or who had received a kidney transplant, we encountered many disorders that had never or only rarely been described before. It was like travelling through space to another planet. As you pointed out, it was thrilling to save people who otherwise would have died. It is hard to describe to someone who wasn't around during that era of medicine just how thrilling successes were and often how bitterly disappointing failures could be.

Dr. Glassock: I agree completely. The combination of curiosity and powerful new tools can be intoxicating.

Dr. Kopple: You stayed in academic medicine—obviously to everybody's benefit—but when did you first consider the possibility of becoming an academician? Did you want to do that before you started medical school or did that begin later in your career? What prompted your decision?

Dr. Glassock: My professional career goals during my last year of medical school were to become a solo practitioner in general internal medicine. That mindset continued during my first few months of internship. I had no particular preference for one discipline over another. I certainly had plenty of exposure and opportunities to look at fields like cardiology or hematology, which were very strong programs at UCLA at the time.

The singular experience described above, with the patient who was dying of a disease that no one could cure, and the transformation that occurred after she received a kidney transplant (compared to her miserable existence on weekly peritoneal dialysis with a temporary catheter) had a powerful influence on my career choice. This young woman was extremely brave, and my experience with her resulted in my abrupt change in focus.

I never intended to pursue a career in a research laboratory exclusively, and I didn't view myself as a laboratory scientist. I always wanted to be involved in patient care in some capacity and looked upon research as an opportunity to explain the problems of real patients.

Dr. Kopple: Would you ascribe any of the inspiration that led you to these decisions to your interactions with Dr. Maxwell, Dr. Merrill, Dr. Goodwin, or to other mentors or role models?

Dr. Glassock: I have had three principal mentors in my professional life who, looking back, had key effects on my career. One was David Solomon, a young UCLA faculty member (an Endocrinologist trained at Harvard) who offered me an opportunity to work part time in his lab when I was a first year resident. David was inspirational from day one and he stimulated my curiosity in research. (He later recruited me to a Faculty position at Harbor-UCLA Medical Center).

Dr. Merrill, my first nephrology mentor at the BWH, was a charismatic person deeply involved in both transplantation and dialysis. He was a world leader in those fields, and everyone looked up to him. I learned a lot about patient care under Dr. Merrill, and without him, I would never have gotten the job with Frank Dixon, who propelled my interest in immunology to a much higher level. The rigors and demands of research as a career really came out in my day-to-day exposure with Dr. Dixon and the trainees he attracted. I still regard him as a brilliant and creative investigator of the highest magnitude.

Dr. Kopple: What events in your career have given you the greatest satisfaction?

Dr. Glassock: Other than the ability to see, analyze, and hopefully help patients, which continues to this day, I think my experience in the discovery of anti-glomerular basement membrane (anti-GBM) disease has to rank at or near the top. In 1964, we had only limited knowledge of autoimmune diseases of the kidney. We suspected they were real, and a lot of experimental evidence in animals had shown the way. So the seminal group of experiments that Richard Lerner, Frank Dixon, and I started in 1965 gave me a great deal of satisfaction. Not only was the work a first, but it helped bring this disorder to light in the minds of many other investigators who went on to make very significant contributions. In the past 50 years, we have gone from the discovery of anti-GBM disease to a cure for many patients—the whole cosmos of discovery to cure encapsulated in a single disease entity. I am very proud of what I was able to contribute to the field in that early experience.

Dr. Kopple: What other achievements gave you great satisfaction?

Dr. Glassock: I had one experience . . . and I wouldn't necessarily say it gave me great satisfaction, but I learned much from it. I studied the pathogenesis of membranous nephropathy (MN), which as you know, has turned out to be another autoimmune disease of the kidney. I worked pretty diligently on that problem—using experimental models. Trying to understand how the disease develops was one of the subjects of my first NIH grants. We carried out a series of well-designed experiments that led us in *one* direction, but it turned out it was not exactly the *right* direction.

Others, such as Bill Couser, actually discovered the true answer to the question of the pathogenesis of this disease. However, if you carefully examine the thread of ideas over 15 or 20 years, they all cumulatively fostered and eventually contributed to the landmark discovery by Laurence Beck, David Salant, and their colleagues in Boston of the anti-phospholipase A2 receptor and its role in human MN.

More recently, in my post-retirement career, I have become very interested in chronic kidney disease (CKD) and the aging kidney. This work has given me a lot of satisfaction, particularly because it has allowed me to write and publish when I might have been spending time tending the roses or walking on the beach. Instead I've been spending time thinking and writing, which is fun and enjoyable for me.

Dr. Kopple: As someone who has not only followed your career, but also watched the evolution of nephrology, your writings in the field of CKD have added a number of dimensions to the way most of us consider this disorder. Over the years, you have added an enormous amount of perspective and wisdom to the way we approach disease.

Dr. Glassock: Thank you, Joel. For those reading this interview who find writing challenging, I want to tell you that I found writing scientific papers incredibly difficult—painful even—in the beginning. But as I gained more knowl-

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edge and familiarity with the literature and read the work of others who were truly great writers, I found it became easier and more enjoyable.

I now relish the opportunity to sit down at a computer and write an analysis, a review, or an original manuscript, which would have been anathema to me when I was in my 20s and 30s. So do not give up hope if you think you can't write. It is an acquired talent that isn't easy, and it does take a lot of practice.

I have done a lot of writing in the hope that it will help people better understand various diseases. Although I may not have always contributed original ideas, I have tried to translate the writings of others into content that is perhaps more digestible and practical to clinicians facing the day-to-day problems of patients with CKD, particularly those with glomerular disease.

Anti-GBM disease and the excitement of the experiments we did in the late '60s still remain among my most treasured memories in the field of glomerular disease research. We utilized knowledge available at the time in experimental laboratories and translated it in a way that led to new diagnostic tests, novel classifications, and innovative therapies that had an immediate and lasting impact on patient care. I am very proud of that.

Dr. Kopple: It may not be well-known, but you recruited me when you were Chairman of Medicine at Harbor–UCLA Medical Center to replace you as Chief of the Division of Nephrology and Hypertension. From time to time, you graciously agreed to speak at our Renal Grand Rounds. I was always impressed that when word got around that you would be giving the lecture, the number of attendees would at least double and many private practitioners in nephrology from the surrounding area would come specifically to hear you. Your talks were extremely informative and scholarly, integrated diverse pieces of information, and invariably provided practical information that could be translated directly into patient practice.

Dr. Glassock: Your point about recruitment speaks to how one becomes a successful leader in academic medicine. One of the fantastic talents of Donald Seldin, one of the great icons of Nephrology, was his ability to find extremely bright and gifted individuals and nurture their careers successfully. I think he has 4 Nobel Prize winners in his Department. I can now claim with some degree of humility that selecting you as my successor was one of the best decisions I ever made.

Dr. Kopple: I am deeply honored by your statement. Along this line, what advice would you give young physicians making decisions about which path to pursue in their professional careers?

Dr. Glassock: I think the most important thing is to find something you love to do. Don't ever choose a path that you feel uncomfortable or unhappy with. There will also inevitably be periods of unhappiness in any career, so don't give up too early. I certainly had doubts about my own career path. My very first independent research activity didn't pan out as successfully as I'd hoped it would and there were many periods of discouragement, but in the end, it's a matter of being happy and satisfied with your choice.

If you want to pursue a career in research and clinical scholarship, you have to maintain a high level of curiosity; be persistent, patient, and resilient; and surround yourself with talented, passionate people and powerful tools. These ingredients for a successful career in nephrology haven't changed. Another ingredient is money in the form of grants or gifts to nurture career development, support investigator-initiated studies and trials, and to promote collaborative engagements. Funding for research and training has been an up-and-down affair over the years, but I don't think that money alone is the key to success in research. You've got to have the curiosity, the persistence, and the tools, and eventually things will come your way.

As far as clinical care is concerned, you have to love being around sick people and have confidence that somehow you can transform their lives for the better. Nephrology provides this in a big way. There are enormous opportunities to do good: transplantation, successful dialysis, diagnosis and treatment of glomerular disease, management of fluid and electrolyte disorders, treatment of hypertension, and so forth. This has been a characteristic of our discipline ever since it was founded, and I think it's just as attractive a discipline today as it was then.

Dr. Kopple: It is said that one attraction of a nephrology career is that nephrologists are often among the best all-around clinicians owing to the demands of the nephrology practice. Nephrologists must not only be specialists in their field, but their patients develop so many different complex, interrelated illnesses that they must have a strong background in other areas of medicine. Do you see it this way too?

Dr. Glassock: I agree with you completely. Nephrologists are great internists and have a perspective in medicine that few other disciplines have. I was Chairman of the American Board of Internal Medicine in the early 1990s, and at that time there was a strong movement to balkanize medicine, to divide it up among its subspecialties and, in a sense, sever the link between the core of internal medicine to allow these subspecialty disciplines to pursue their own development without any firm linkage to the mother discipline. I would be very unhappy if nephrology ever became divorced from internal medicine and I hope that some of my efforts to prevent this were successful.

The knowledge I've gleaned from nephrology is often very applicable to common problems seen in internal medicine. Even today when I see patients without nephrology-related problems (and I do see such patients from time to time), my knowledge of nephrology is very useful.

Dr. Kopple: How can we best make nephrology more attractive to potential trainees or fellows?

Dr. Glassock: We can communicate the fact that opportunities for the pursuit of knowledge have never been greater. Gene technologies and bioengineering—which were unimaginable a few years ago—are on the cusp of being applied to patient care. Such technologies can lead to excitement, and excitement leads to interest. So communicating the opportunities in clinical scholarship to the next generation of nephrologists is key.

We need to focus on the origins of some practitioners' dissatisfaction with nephrology and see whether the factors that are controllable can be modified. I don't think dissatisfaction with nephrology as a career stems from its lack of intellectual challenges. There are many intellectual challenges and opportunities in nephrology.

Money, I think, unfortunately, is one of the main reasons for dissatisfaction. One obstacle that didn't exist 30 or 40 years ago is the burden of debt. Medical students and residents come out of medical schools and training programs deeply in debt, and this can't help but influence their career choices to an extent. Inheriting so much debt and then having to struggle to resolve it in the face of reduced reimbursement places additional demands on practices that make for dissatisfying careers.

Medicine has become a business and that tends to divorce you from the day-to-day care of your patients. The patients have also changed. In dialysis units, we deal a lot with older patients with multiple comorbidities and often depression. Oncologists also deal with older patients with diseases that lead to desperation—yet they have among the highest career satisfaction. I believe this is partly because they now can really do something to take care of their patients and see results. I think we can too. I just don't think we are communicating and showing it as well.

Dr. Kopple: I remember when we could not treat people dying of chronic kidney failure with dialysis, and of course transplants could only be done occasionally during the early '60s. To this day, every time I start a patient with ESRD on dialysis, I feel it is a miracle that I can do something now that could not be done when I was a student. It is like giving life to someone who otherwise would not have a future. Having said that, as you pointed out, chronic dialysis patients are often very depressed and anxious. I wonder whether the experience of many medical students and young doctors with depressed or anxious chronic dialysis patients discourages the former from going into nephrology.

Dr. Glassock: Training of young residents has been very hospital-centric for many years. That's beginning to improve with more mandatory outpatient assignments, but can you imagine the viewpoint of a young internal medicine resident looking at nephrology as a career but seeing only those patients who are

too sick to be managed as an outpatient? They may not always get to see that many patients on renal replacement modalities have very reasonable lives.

You've referred to me patients who did magnificently on dialysis, but they were never in the hospital, so no residents ever saw them. If we want to encourage the next generation of nephrologists, we must find a way for these young people to see the discipline practiced in its broadest sense, not just a snapshot within the artificial environment of a hospital.

Dr. Kopple: You are saying that we need to rethink the way we organize training programs, not just for nephrology fellows, but also for residents who are still considering which specialty they may want to pursue.

Dr. Glassock: Peer interaction also has not gotten as much attention as it should. My peers—people like Barry Brenner, Alan Hull, Tom Parker, Claudio Ponticelli, Bernie Carpenter, and yourself, as well as the numerous trainees that I supervised over my career—had a huge influence on my professional development. Opportunities for discussion arose whenever I was among these people, and we all inspired each other. The interactions I had and continue to have with my peers provide reassurance and confirmation that within the discipline of nephrology, the sum is greater than the parts.

So isolation from the broader sphere of nephrology can be a great detriment to professional development. Physicians considering nephrology as a career should take advantage of every opportunity to develop mutually constructive relationships with their peers. This is possible now, much more than in the past, because of new technologies like the internet and social media that encourage these kinds of relationships.

Dr. Kopple: Where do you see nephrology going in the future? If you were to look ahead 50 or 75 years from now, what do you think nephrology will be like?

Dr. Glassock: I think we are going through a transitional period in which the primacy of dialysis as a major part of nephrology will diminish. You can see this vividly in evaluations of the global burden of dialysis—at least for developed countries like the US, not for underdeveloped countries, which may be decades behind. In America, I think the future of nephrology will see dialysis occupying a less major role in patient care.

Transplantation, on the other hand, will become a much more dominant part of the renal replacement portfolio because of changes in management and the fact that the ability to produce permanent tolerance is likely to occur in the next few decades.

So if I were to look at what nephrology will be like 50 years from now, dialysis will not be as common, transplantation will still be very important, and the variety of tools available for clinical nephrologists to prevent and treat diseases before they get to the end stages will be enormous. I also do not think diabetes or diabetic nephropathy will be a major problem 50 years from now.

You might ask, "What's going to happen to nephrology if we don't have any diseases to treat?" Isn't that our goal anyway? There will always be disorders that arise that we don't even know about, like Mesoamerican nephropathy or a Zika-like virus that causes kidney disease, for example. These are inevitable, but going forward, we will do a better job of taking care of patients and preventing end stage renal disease.

Also, of course, we are learning that some patients have nothing to benefit from beginning dialysis. For the frail elderly, dialysis may not be the best option. Palliative or conservative care may be as good or better.

Dr. Kopple: Do you think there will be new sources of kidneys for transplantation?

Dr. Glassock: The hope is that we can bioengineer a fully compatible kidney on a decellularized non-human kidney scaffold by implantation of embryonic stem cells directed to differentiate into the nephron segments. For the moment, I think that's a bit of magical thinking. No one to my knowledge has yet achieved anything close to a functional kidney via a bioengineering approach. But the principles are reasonable, and if we can overcome some of the present seemingly insurmountable obstacles, I think it's theoretically possible that we will eventually do away with the need for living donor and deceased donor transplants.

Dr. Kopple: What about preventive nephology and public health measures?

Dr. Glassock: We have a very promising arena for preventing acute kidney injury (AKI) in underdeveloped countries. AKI is often related to diarrhea, infectious diseases, and community-based toxic exposures. If we can improve the water supply and early treatment of diarrhea and infectious diseases like malaria and leptospirosis, if we can eliminate snake bites and the like, then yes, we could make major inroads in AKI in underdeveloped countries.

As for CKD, yes, we can do a great job with prevention. But I'm not convinced that large-scale screening is the approach we should take. I'm more inclined to believe our approach to prevention will become more nuanced and targeted to specific diseases recognized by molecular techniques or other forms of genetic analysis rather than screening a seemingly healthy population for markers of disease. Essentially, I think prevention is going to be a dominant part of our discipline as we learn more about the genetic and immunologic origins of the diseases we are now treating. The better we get at identifying the pathogenesis of disease, the better equipped we will be to prevent it.

Dr. Kopple: It has been pointed out that about 70–72% of people with end stage kidney failure have diabetes, hypertension, or other, obesity-related kidney diseases as the cause of their kidney failure. Do you think there could be a major role for public health measures to reduce the contribution of these disorders to end stage kidney disease, particularly because one should be able to prevent many of these conditions?

Dr. Glassock: In principle, your concepts are quite defensible. In practice though, I think we have overestimated the ability of physicians to alter behavior in a manner that will prevent diseases. You're talking about a fundamental change at a societal level of the factors that are believed to have contributed to these common diseases, such as overeating, lack of exercise, consuming too much salt and the wrong kind of calories, too much smoking . . . that all involves a behavioral change in the patient starting when they appear healthy.

I have kids who believe they're immortal. I believed I was immortal when I was their age too. Convincing them to change their behavioral habits in order to glean a benefit at the end of their life is very difficult. Although you are right about obesity, overeating, and under-exercise, translating that knowledge into an effective tool to prevent disease is an extraordinarily difficult and often unsuccessful effort. There is a 90% recurrence rate after treatment for obesity. Unless we eventually learn to better understand exactly what causes obesity (and it is a very heterogeneous disease, like so many, that will have to be dissected into its various components), some treatments will work for some but not necessarily for others. So I agree with you in principle, but in a pragmatic way, I'm less fully convinced.

Dr. Kopple: I might make a minor dissenting point. Obesity was much less prevalent in the United States and other countries until sometime around the 1970s—the pandemic of obesity is quite recent. When I watch old movies made before the mid- or late 1960s, it's fascinating how much thinner people generally were. It's my hope that we might be able to change our eating patterns and in some ways revert back to the way we used to be.

I completely agree that the treatment of obesity, other than perhaps by bariatric surgery, gives poor results. Perhaps we can develop educational programs and other societal tools for preventing people from becoming obese in the first place. This is my hope.

Dr. Glassock: Let me use a personal example. When I started out in nephrology and dialysis, a major cause of end stage renal failure was glomerulonephritis. Most patients considered as candidates for renal replacement therapy, and young patients in particular, had glomerulonephritis. Back then, we didn't dialyze any diabetics. But look at today—glomerulonephritis as a cause of end stage renal failure is decreasing in many parts of the world.

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So if you understand the mechanisms of the disease processes that lead to end stage renal failure, you can eventually deliver effective tools to manage it. Glomerulonephritis, which is my field of expertise rather than obesity, is a prime example of that precept. Better tools for detection, classification, and management of glomerulonephritis will logically form a better understanding of the disease processes and lead to better outcomes.

Anti-GBM disease is now often curable, as patients can go into long-term remission if the disease is detected early enough and treated appropriately. That accomplishment happened over the past 50 years. It took the efforts of many investigators and brave patients, but this, I think, is the paradigm of how one needs to pursue the diseases that cause end stage renal disease today. That's why I'm so optimistic about the future of nephrology, because the great achievements that have occurred in glomerulonephritis have and are occurring in hypertension, diabetes, and obesity.

Dr. Kopple: There is another cause of progressive kidney failure: as people age, they usually lose a large proportion of their glomerular filtration rate. This is associated with histological changes within the kidney. Do you see advances occurring in this area as well?

Dr. Glassock: That's a good question, and I've spent a lot of time thinking about it. Organ senescence, as it occurs in the kidney, is a loss of nephrons over time. We've documented that from measurements of the number of nephrons remaining in peoples' kidneys as they get older. The origin of renal senescence is very complicated, and I think we're only beginning to understand it.

The rate of renal senescence may begin in utero. You're born with a certain number of nephrons. Barry Brenner has been the leading force in demonstrating the relevance of this to human biology. However, no two individuals are alike with respect to the number of nephrons they have at birth. Some have very few and some have too many. This is all conditioned on the fact that intra-uterine nutrition modifies nephrogenesis, and it is manifested by low birth weight. Low birth weight and low nephron endowment predict, in my opinion, the eventual impact of renal senescence and loss of nephrons later in life. If this hypothesis is true, and you happen to be born with a weight <2.5 kilograms, my prediction is that the effect of renal senescence will be greater because you started out with fewer nephrons.

If this idea translates into reality—and it hasn't yet—it may offer an opportunity to alter the rate of renal senescence going forward by eliminating a treatable disease—intrauterine fetal malnutrition. We're not always going to have the greatest tools to do that, but we can help prevent fetal malnutrition by improving maternal nutrition. I think you can grasp the significance of this hypothetical framework about what it means to lose nephrons over one's lifespan and how important it is, in my opinion, to ensure that you're born with the most nephrons possible and to protect those nephrons to the maximum extent throughout life. I believe attention to this approach will have an impact on the rate of CKD as it appears in populations studied by epidemiologists.

Dr. Kopple: That's a very interesting perspective. Before we close, are there any final comments you would like to make?

Dr. Glassock: I want to congratulate ASN and the leaders who decided to allow us old-timers to tell our stories. I hope my optimism will encourage at least one individual on the cusp of making a decision about where to go with their medical career to choose nephrology. I can assure them that if they take this choice seriously, they will not be disappointed and that the future of nephrology is golden and bright. If they just put themselves in the right place at the right time with a heavy dose of curiosity, they will have a wonderful lifelong experience with this magnificent and noble profession we call nephrology.