ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

Kidney News

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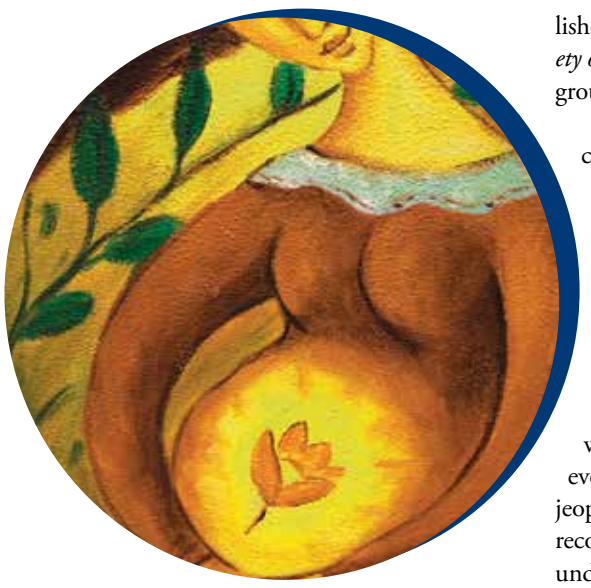
Prior Acute Kidney Injury May Contribute to Adverse Pregnancy Outcomes



Acute kidney injury (AKI) is most often considered a concern for elderly and critically ill populations, but a new study indicates that it may also pose risks for pregnant women and their babies, even when women have recovered their kidney function before pregnancy. The findings, which are published in the *Journal of the American Society of Nephrology*, point to a newly defined group of high-risk women.

Previous research has shown that AKI can increase the risk of later developing chronic kidney disease (CKD) and dying prematurely, but the consequence of an episode of AKI on health outcomes relevant to young women—especially those who may become pregnant—has not been addressed fully. Several studies have reported adverse pregnancy outcomes in women with early stages of CKD, and even subclinical kidney dysfunction may jeopardize healthy pregnancies. Therefore, recovered AKI (r-AKI) may represent an under-recognized threat to women who wish to bear children.

To study whether a history of r-AKI increases a woman's risk of later problems during pregnancy, Jessica Sheehan Tangren, MD, a Research Fellow in the Division of Nephrology at Massachusetts General Hospital, and her colleagues retrospectively studied all women who delivered infants between 1998 and 2007 at her institution: 105 women with r-AKI and 24,640 women without a history of kidney disease.

Women with r-AKI had an increased rate of preeclampsia compared with controls (23% vs. 4%). Also, infants of women with r-AKI were born earlier than infants of controls (average 37.6 vs. 39.2 weeks), with increased rates of small-for-gestational-age births (15% vs. 8%) and newborns admitted to the neonatal intensive care unit (26% vs. 8%). There were 189 perinatal deaths in the cohort, with significantly more deaths in the offspring of mothers with recovered AKI (3.0% vs. 0.8%); however, this association became non-significant in a multivariate logistic regression analysis.

Recovered AKI was linked with a 5.9-times increased risk of preeclampsia and a 2.4-times increased risk of adverse fetal outcomes, after adjustments were made for various patient factors including maternal age, body mass index, race, parity, history of diabetes, and diastolic blood pressure at first prenatal visit. When women with r-AKI and controls were matched 1:2 by age, race, body mass

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Older Age Should Not Rule Out Organ Donation after Death, According to New Research

By Tracy Hampton

New research indicates that age cut-offs for deceased organ donors prevent quality kidneys from being available to patients in need of life-saving transplants. Even kidneys from donors ≥80 years of age functioned for years after transplantation in a recent *Clinical Journal of the American Society of Nephrology* study.

"Nowadays, in many countries, about 30% to 60% of deceased kidney grafts are included in the so-called 'extended criteria.' However, as witnessed by the heterogeneity of organ discard rate across the transplant community, the limits of this policy are not well defined despite the development of several scoring systems," the study authors wrote. They noted that donor age in particular represents a major reason for organ discard, but data on the reliability of organs from elderly donors are currently limited and relevant studies have generated conflicting results.

The donor organ shortage has led to recent efforts to find ways to expand kidney recovery criteria, however, including the consideration of older deceased donor kidneys. Strategies incorporating such kidneys include *old* for *old* protocols that aim to match the estimated graft survival to

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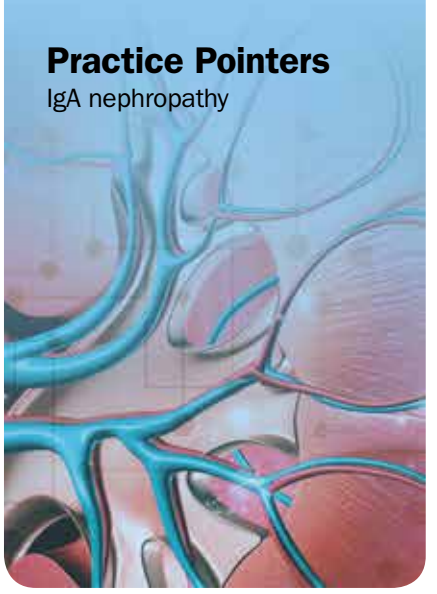
Inside



ASN, CDC Effort to Prevent Dialysis Infections Addressed at Kidney Week Town Hall

Infections are now neck and neck with cardiovascular complications as a primary reason for hospitalization and mortality among kidney patients receiving dialysis. To help counter this trend, ASN recently partnered with the US Centers for Disease Control and Prevention (CDC) to develop the Nephrologists Transforming Dialysis Safety (NTDS) Project to promote infection prevention in outpatient dialysis facilities.

The project is funded by a 3-year contract with the CDC that began July 15, 2016. ASN convened a town hall to inform and receive feedback about NTDS from the kidney community at Kidney Week in Chicago in November 2016.

"We must aim for reduction and eventually elimination of infections," said Alan Kliger, MD, NTDS project committee chair. Kliger is affiliated with the Yale New Haven Health System.

Patients undergoing maintenance hemodialysis are at a high risk for infection because their treatment requires frequent use of catheters or insertion of needles to access the bloodstream. Dialysis patients often have changes to their immune systems, making them more prone to infections, and for some, frequent hospitalizations expose them to healthcare-associated infections (HAI).

Key goals of NTDS are to

- promote better dissemination and implementation of existing CDC infection control guidelines in dialysis facilities,
- provide better education and tools to clinicians and trainees to stop infections from developing,
- establish antibiotic stewardship programs for dialysis facilities, and
- develop stronger ties between nephrologists and HAI experts at the state and federal levels.

"The CDC has developed tools and special procedures, yet the incidence and mortality from infections has not changed," Kliger said. "This [effort] needs to be very special work with dialysis centers, with the nephrologist as leader, chair of the team, not just relying on other healthcare workers such as nurses or technicians to report infections."

Strategies to engage nephrologists in infection control efforts as part of NTDS will include collaboration with dialysis companies, development of continuing medical education (CME) programs that emphasize infection prevention, and work with academic training programs to educate and train nephrology fellows.

The project includes nephrologist representatives from two of the largest dialysis companies (LDOs), as well as adult and pediatric nephrologists from small dialysis companies (SDOs), and academia, infectious disease specialists, hepatologists, state HAI program representatives, dialysis nurses, dialysis technicians, CDC, and ASN Council.

Kliger noted that Methicillin-resistant Staphylococcus aureus (MRSA) infections are 100 times more likely, and hepatitis C infections, 5 times more likely, in maintenance dialysis patients than in the general US population. Also common in dialysis units are infections from vancomycin-resistant enterococci and other multidrug-resistant organisms.

Four workgroups will provide clinical expertise and direction to the NTDS Project: Quality Assessment, Improvement, and Education (QAIE); Training Programs; State and Federal Health-Acquired Infections Programs; and Current and Emerging Threats.

QAIE chair Leslie Wong, MD, MBA, FASN, said the current state of infection control in dialysis facilities is untenable. Wong is Vice Chairman of Nephrology and Director of the End-Stage Renal Disease Program at the Cleveland Clinic.

"Infections consume our energy, resources, and most importantly the lives of our patients," Wong said. "We know how to prevent infections, but we won't, can't, or don't do it. It's just not acceptable. I do not want to practice in this environment for the rest of my career."

Wong noted that many facilities in the US are cited repeatedly for infection-related events. "When you mention compliance in the dialysis facility, it immediately evinces negative remarks," he said. To change this culture, "we need to start with a needs analysis, root causes, leadership, organizational behavior, and patient engagement."

The QAIE Workgroup is planning a series of infection prevention webinars as well as infection prevention symposia at ASN Kidney Week meetings in 2017 and 2018. The workgroup also hopes to develop educational tools and to dialogue with national dialysis organizations about medical director leadership training and preparedness, the Virtual Mentor Dialysis Curriculum, and support from CDC's National Healthcare Safety Network.

Training Program Workgroup chair Sharon Adler, MD, said one goal of the Training Program Workgroup is to develop educational tools with similar content for use by both fellows and practicing nephrologists. Adler is chair of the education committee at the Harbor-UCLA Medical Center Division of Nephrology.

The workgroup also aims to secure accreditation for infection control training and to provide an update to the American Board of Internal Medicine nephrology blueprint regarding inclusion of knowledge about infection prevention in dialysis units on the Nephrology initial certification and maintenance of certification exams. Also under consideration is a proposed emphasis on education to reduce the use of catheters, called "Target Zero Catheters."

"We would like to examine the barriers in going from catheters to fistulas," Adler said.

Kidney care professionals need to familiarize themselves with state and federal programs for healthcare-associated infections (HAI), said Anitha Vijayan, MD, FASN, of the Division of Nephrology at Washington University in St. Louis. Vijayan co-chairs the NTDS Workgroup on State and Federal HAI Programs with Eugene Livar, MD, Healthcare-Associated Infections Program Manager, Arizona Department of Health Services.

"We must engage nephrologists, not just dialysis nurses, to report infections," Vijayan said. "Not a lot of state HAI programs include dialysis units."

Vijayan said the workgroup hopes to develop a directory of state-level HAI program contacts and educate state and federal HAI programs about NTDS.

T. Alp Ikizler, MD, of the Vanderbilt University School of Medicine Division of Nephrology and Hypertension, co-chairs the NTDS Current and Emerging Threats Workgroup with John Boyce, MD, infectious disease specialist, Middletown, CT. One of the workgroup's first tasks will be to perform a "gap analysis" of dialysis units' response to Ebola as a case study for emerging threats.

"We will communicate with SDOs and LDOs to know what they are doing [regarding emerging threats]," Ikizler said.

Other areas of focus include an increased emphasis on basic infection control protocols such as hand hygiene, dissemination of existing guidelines for hepatitis B and C, and identification of infection control issues that lack clear guidance.

"What about isolating patients with infections?" Kliger asked. "The Centers for Medicare & Medicaid Services is clear on hepatitis B isolation, but not for other multidrug-resistant organisms that are transmissible."

"We definitely need more input and research on these areas to determine what is effective and feasible," said the CDC's Priti Patel, MD, MPH, of the CDC's Division of Healthcare Quality Promotion, and CDC liaison for the NTDS project.

Dialysis units' response to multidrug-resistant organisms and level of antibiotic stewardship will also be under the purview of the Current and Emerging Threats Workgroup."We have programs [for antimicrobial stewardship] in hospitals but not in [freestanding] dialysis units," said Kliger. "We must think globally to prevent multidrug-resistant organisms from spreading. We also need to think about the effects of antibiotics on the patient's gut microbiome."

NTDS will engage nephrologists, ancillary healthcare providers, health departments, and other stakeholders to implement best practices that will safeguard dialysis patients against infections. "We need to look at what we know is best and change the culture to use these practices," Kliger said.

"It's not an issue of having the right tools out there," said QAIE Workgroup chair Wong. "It's about the transformation of health care in general. We grew up in medicine thinking that we just gave orders to others to get the best outcomes for our patients. We have to realize that health care is a system and that we have to work within that system. Do we inspire or do we deter these practices from happening?"

Pregnancy Outcomes

Continued from page 1

index, diastolic blood pressure, parity, and diabetes status, r-AKI was associated with a 4.7-times increased risk of preeclampsia and a 2.1-times increased risk of adverse fetal outcomes. A similar association between r-AKI and adverse pregnancy outcomes was observed in analyses excluding all women with diabetes, obesity, and hypertension.

"We believe that this study highlights an important finding that will be useful for medical providers caring for reproductive-age women," Tangren said. In particular, health care providers should consider the study's findings when counseling women with previous AKI—not just those with advanced preexisting kidney disease—about the risk of adverse outcomes in pregnancy.

The investigators stressed that the interaction between diseased kidneys and the feto-placental unit during gestation remains unknown and requires additional research. They hypothesize that in women with prior AKI, subclinical vascular endothelial injury may sensitize the vasculature to the toxic effects of circulating antiangiogenic factors that rise prior to term in all pregnancies. Additional animal and human studies are needed to test this potential explanation, however. "Our goal in future studies is to address why women with a history of AKI are at higher risk for pregnancy complications and to identify strategies to lower their risk," Tangren said. They also would like to know if AKI severity is associated with future preeclampsia risk. In this study, because there were a small number of events in each AKI stage, the investigators did not have the power to address this relationship.

The varying rates of preeclampsia reported worldwide may be explained, at least partially, by the study's findings, Tangren noted. Preeclampsia rates range from 1% to 15%, with higher rates reported in low-income countries. Also, rates of AKI are higher among young women in low-income countries.

Giorgina Piccoli, MD, who was not involved with the study and is the Chair of the Division of Nephrology at the University of Torino in Italy, noted that the cross-talk between the kidney and the placenta is important. "[It is] no wonder perhaps if all types of kidney damage are reflected and amplified in pregnancy, a situation in which the kidney is under functional stress," she said. "The study's findings are in line with previous studies of our group and others that suggest an effect of even minor renal damage in the development of adverse pregnancy-related outcomes. I'm concerned about how many patients we do not follow as high-risk pregnancies, and about how much we have to do to offer the best treatment to all of our patients."

The article, entitled "Pregnancy Outcomes Following Clinical Recovery from Acute Kidney Injury," appeared online at http://jasn.asnjournals.org/ on December 22, 2016, doi: 10.1681/ASN.2016070806.

Older Age

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recipient life expectancy and dual kidney transplantation that is intended to compensate for the limited nephron mass of older donor kidneys.

To see how donor age affects the long-term functioning of transplanted kidneys, Luigi Biancone, MD, of the University of Torino, in Italy, and his colleagues retrospectively analyzed information on all deceased donor kidney transplants performed at the Turin University Renal Transplant Center over an 11-year period from 2003 through 2013, with kidney transplants from extended criteria donors classified according to donor age classes. In the first study specifically focusing on donors ≥80 years old and dividing extended criteria donor cohort into decades, the team assessed the most relevant long-term outcomes together with associated risk factors.

The investigators excluded multi-organ grafts from 1199 consecutive transplants. Of the remaining 1124, there were 647 kidney transplants from extended criteria donors, which were defined as all donors >60 years and those aged 50 to 59 years with ≥2 of the following characteristics: serum creatinine at procurement >1.5 mg/dL, cerebrovascular cause of death, and history of hypertension.

After a median follow-up of 4.9 years, patient and kidney survival rates were comparable among the 4 age groups considered (50–59 years, 60–69 years, 70–79 years, and ≥80 years). The 5-year patient survival rates ranged from 87.8% to 90.1% in these age groups, and the 5-year kidney survival rates ranged from 65.9% to 75.2%. Patient and graft survival rates were comparable between dual and single kidney transplants, except for the ≥80 year age group, which had better graft survival with dual kidney transplantation.

Donor age classes did not correlate with most adverse events, including vascular and urological complications, new onset diabetes, and malignancies. Acute rejection rates were also comparable in the 4 groups, whereas infection rates appeared to be lower in the ≥80 year age group, particularly for cytomegalovirus infection (11.1% vs. 26.4% of group 1, 31.8% of group 2, and 28.3% of group 3).

"The results of this study support the use of extended criteria donors, even donors older than 80 years, but they have to be accurately selected and managed with dedicated protocols," Biancone said.

Rates of kidney discard before transplantation were similar for kidneys from donors in the 3 younger age groups (15.4%, 17.7%, and 20.1% respectively), but the discard rate was strikingly higher (48.2%) among kidneys from octogenarian donors. Most of the reasons for discard were age-related; in particular, macroscopic flaws and Karpinski score >6 were found in 20% and 11.8% of organs harvested from donors ≥80 years vs. 4.8% and 3.7% of those from the youngest extended criteria donors.

"Kidneys from octogenarian donors, which currently represent a significant proportion of the donor pool, are discarded in almost 100% of the cases by many transplant centers," said Umberto Maggiore, MD, who was not involved with the study and is a transplant nephrologist at the University Hospital of Parma, in Italy.

"This study provides findings that might help transplant physicians for decision-making purposes," Maggiore said. "I would summarize this with a simple rule of thumb, called the 'half rule,' as follows: using histological parameters (in this study a dedicated renal pathologist evaluated a formalin-fixed needle biopsy using the Karpinski score), half of the kidneys will be discarded; of those recovered, almost *half* of the donors will be eventually used for dual transplantation, the 5-year cumulative incidence of graft failure of those allocated to dual transplantation being *half* compared with single transplantation."

Other evaluation tools—such as those that analyze vascular resistances and perfusate biomarkers during kidney machine reconditioning or donor urinary biomarkers for ischemia-reperfusion injury—may allow for an accurate allocation of organs from elderly donors.

The article, entitled "Long-term Outcomes and Discard Rate of Kidneys by Decade of Extended Criteria Donor Age," appeared online at http://cjasn.asnjournals.org/ on December 15, 2016, doi: 10.2215/CJN.05990616.

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Policy Update

Prize Competitions to Spur Medical Innovation and Patient Voice in FDA Approvals May Benefit under 21st Century Cures Act

In late 2016, Congress passed and President Barack Obama signed into law the 21st Century Cures Act, a sweeping medical innovation bill authorizing more National Institutes of Health (NIH) funding and supporting patient perspectives in U.S. Food and Drug Administration (FDA) approvals.

ASN advocated for these and other provisions in the new law, including calling on the NIH to support prize competitions to improve patients' lives in fields where there is a significant disease burden, or where current investment is disproportionately small relative to federal costs. With 20 million Americans with kidney disease and over 600,000 with end stage renal disease (ESRD), Medicare spends over $80 billion annually providing care for kidney patients. The NIH investment in kidney research of $585 million is less than 1% of Medicare kidney care expenditures.

At the White House Organ Summit in June 2016, ASN pledged the first $7 million toward a prize competition to develop a novel wearable or implantable device that replaces kidney function and improves patient quality of life. The new law may facilitate collaboration with NIH as ASN seeks to launch the prize competition in 2017.

"21st Century Cures' call for NIH to support prize competitions for the development of novel therapies could help revolutionize kidney patient care," said ASN President Eleanor D. Lederer, MD, FASN.

The $6.3 billion bipartisan law is also designed to help find cures for cancer, provide $1 billion to fight opioid addiction, treat mental illness, and better understand the brain to prevent diseases like Alzheimer's. Specifically, the Cures Act provides multiyear funding for three highly innovative scientific initiatives: the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, the Precision Medicine Initiative (PMI), and the Beau Biden Cancer Moonshot. It also includes a promising new research initiative focused on regenerative medicine.

In a *New England Journal of Medicine* article titled "The 21st Century Cures Act—A View from NIH," NIH Director Francis S. Collins, MD, PhD, and NIH Deputy Director for Science, Outreach, and Policy Kathy L. Hudson, PhD, write about measures in the Act that reduce red tape and nurture data sharing while protecting privacy.

"Sharing data is essential for progress in biomedical research," Collins and Hudson write. "Rapid data sharing was key to the success of the Human Genome Project, and that same commitment has been spreading across biomedicine in the past two decades, as advances in technology and 'big data' have enabled an entirely new level of data sharing and inquiry. Despite the clear value of sharing data, the NIH has been constrained from requiring in a straightforward way that NIH-funded investigators share their data. The Cures Act solves this problem by allowing the NIH director to require that data from NIH-supported research be shared, giving all scientists the opportunity to use these data as quickly as possible to advance biomedical research."

The Cures Act's provision of support for patient perspectives in the FDA approval process is in line with an important aim of the Kidney Health Initiative (KHI). The KHI is a public-private partnership between the ASN and the FDA whose membership includes patient groups, health professional organizations, dialysis organizations, pharmaceutical and device companies, and government agencies.

"A pivotal aspect to be realized through the Act is the capacity to collaborate and promote appropriate innovations based on the experiences and perspectives of patients," said James A. Sloand, MD, FASN, senior medical director at Baxter Healthcare and member of the board of directors for the KHI. "The mission of the FDA is to advance therapies and promote public health while ensuring the safety, efficacy, and high quality of novel drugs and medical devices. Given the chronicity and severity of kidney disease, patients' knowledge, experience, and desire for self-determination are recognized as important factors in FDA deliberations. FDA has previously sought earlier and greater input from patients in the discernment process for drug and device approval. The 21st Century Cures Act supports this valuable exchange so that the patient's voice is now fully heard and carefully considered in the product approval process."

Sen. Lamar Alexander (R-TN), chair of the Health, Education, Labor and Pensions (HELP) Committee, called the bill a "Christmas miracle … that will help virtually every American family." The Cures Act passed the Senate by a vote of 94–5 and the House by a vote of 392–26.

To accomplish such large bipartisan votes in both chambers, the chairs of each committee in the Senate and House had to work closely with the ranking Democrats on their committees—and they did. ASN publicly thanked Senators Alexander and Patty Murray (D-WA) of the Senate HELP Committee and House Energy and Commerce Committee Chairman Fred Upton (R-MI) and Democrats Frank Pallone (D-NJ) and Diana DeGette (D-CO).

The year 2017 holds a number of challenges and opportunities for kidney health care providers. In this pair of articles, ASN President Eleanor Lederer, MD, FASN, and leading US dialysis organization CMOs take a look at the state of kidney care at the end of 2016 and where we are headed in 2017 and beyond.

US Dialysis Provider CMOs: **State of Kidney Care 2016**

By Allen R. Nissenson, MD; Franklin Maddux, MD; Doug Johnson, MD; Tom Parker, MD; and Brigitte Schiller, MD, on behalf of the US Dialysis Organization CMOs

Kidney care in the United States is undergoing a rapid transformation as the primary payer, Medicare, moves from volume-based, fee-for-service payment systems to value-based payment systems. Nearly 50% of current CMS payments are based on value delivered, and by 2020 this is likely to be over 90%.

The ESRD program has been at the forefront of these changes because of its heavy dependence on Medicare as a primary payer, its unique position as a disease-specific entitlement, and the high clinical complexity and cost of the patient population. Together, these circumstances create a great opportunity for the discipline of nephrology and all nephrologists to help shape care delivery and payment for kidney patients as well as other complex chronically ill populations, creating significant improvements in patient outcomes, while responsibly stewarding resources. There are a number of challenges in the coming year from the perspective of dialysis provider chief medical officers (CMOs).

1 Transformation of the health care system and transformation of the practice of nephrology

There is no question that systemwide transformation is occurring in the US and globally in the view of providers and payers for healthcare. The movement from volume to value, whereby providers are increasingly accountable for clinical outcomes as well as the total costs of care, is occurring rapidly.

Nephrologists need to be leaders in this new healthcare world and to be successful will need to understand the principles of population management as well as the specific clinical management and care coordination needs of individual patients. Although in the past this evolution of the practice of medicine was like the unicorn—frequently spoken about but rarely seen—it is now clearly happening in nephrology and nephrologists need to be prepared to lead programs and systems of care to ensure the best outcomes for kidney patients.

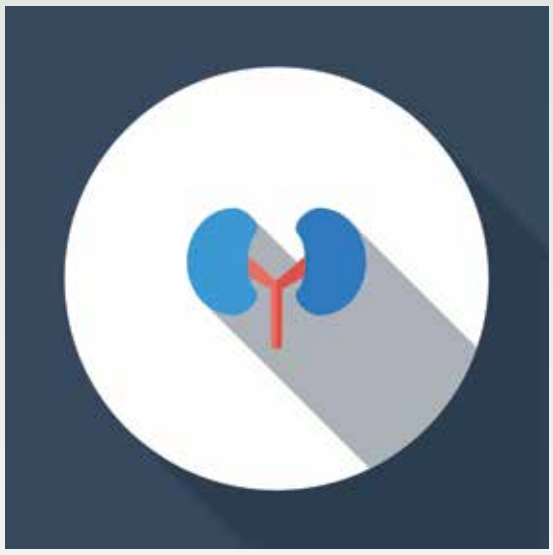
2 Where do nephrologists and dialysis providers fit in the new healthcare system?

Nephrologists and dialysis providers will be at the forefront of the new healthcare system owing to the disproportionate cost of advanced CKD and ESRD patients. Innovative solutions for improving care and controlling costs will be needed going forward. Nephrologists and dialysis providers will need to work together to ensure that these solutions are identified, tested, and implemented.

Nephrologists in the future will have more options regarding their clinical work environment, with an increasing number likely to find salaried positions with health systems, integrated health care organizations, physician groups, hospitals, or dialysis providers. Career counseling needs to be broadened to inform nephrologists of the benefits and pitfalls of these options. In addition, integral to the success of integrated care is the ability to seamlessly share patient information through electronic health records. Nephrologists need to work closely with other providers to design more usable systems and algorithms to enhance such sharing of information in a real-time fashion.

3 The nephrology workforce

The care of patients with CKD and ESRD will be dependent on teams of individuals, including, but not limited to, nurses (RNs and nurse practitioners), social workers, care coordinators, patient care navigators, health coaches, patient care technicians, clinical specialists (e.g., podiatrists, cardiologists, endocrinologists, vascular surgeons), insurance/benefits experts, and others who focus on the social determinants of health, such as housing, nutrition, transportation, and employment. The nephrologist needs to be the leader and coordinator of this team.



There is considerable concern that the decrease in matched Fellows and increase in international medical graduates (IMGs) will make it difficult to achieve sufficient numbers and quality of nephrologists in the future to meet the needs spanning clinical and administrative functions. It is our hope that interest in the practice of nephrology will increase as the role of the nephrologist changes.

4 Integrated care and the ideal role of the nephrologist

It is useful to think about the role of the nephrologist caring for CKD/ESRD patients from the perspective of the site of focus of care.

In the dialysis facility, nephrologists serve as the population health leader when acting as a facility medical director. In addition, nephrologists play an additional role as the principal care provider for each patient for whom he or she is responsible. This role is distinct from primary care, and training programs need to educate nephrologists on these distinctions including roles and responsibilities for each.

Outside the dialysis facility, nephrologists are now likely to be even more involved in care coordination, particularly with the new Quality Payment Program (QPP), which incentivizes participation in care coordination. The QPP, the outgrowth of the Medicare Access and CHIP Reauthorization Act, provides an opportunity for nephrologists to align financial incentives with clinical imperatives. It is essential for nephrologists to understand the impact of nontraditional co-existing diseases so prevalent in kidney patients, as well as the effects of conditions or social circumstances on the health outcomes of the kidney patient. This requires the nephrologist to be more involved in the overall assessment and care of patients, serving as the principal care physician.

5 Influence of regulatory oversight and public data on patient care

There is extensive literature on the impact of publicly reported health outcomes (PROMs) on physician behavior and quality of care. Clearly the results are mixed, and few data are available in nephrology. There is a need for increasing rigor in the development and selection of quality metrics to be used in such systems so that the unintended consequence of judging quality on irrelevant metrics does not drive resources to be devoted to things that don't really impact quality of patient care.

While such oversight of quality in the payment system through the Quality Improvement Program (QIP) has been one of the primary approaches by CMS, further refinement of measures and methodology used to calculate the QIP measures needs to be informed by evidence, sound methods, and in the future include PROMs. Continued engagement of the nephrology community in such accountability systems is essential. Finally, accountability of nephrologists should also be an area developed and structured through the discipline, not by regulators.

6 How evolution of the ESRD prospective payment system affects innovation in the kidney space

There is no question that the introduction of the bundled payment system has had a chilling effect on pharmaceutical and device innovation for kidney patients. Uncertainty about reimbursement potential for new products fosters reluctance for commercial entities to invest. Of note, however, is the more recent renewal of interest in innovation as integrated care systems for kidney patients grow. In such settings, any innovation that creates value generates interest. For example, a more expensive dialyzer is a valuable investment in an integrated care setting if the result is a healthier patient who lives longer and does not require hospitalization. Manufacturers understand this and are starting to react slowly. Removing regulatory barriers to innovation is an important driver of innovation for the future. An assessment of the clinical trials and technology advancement in therapies and pharma would help provide data to assess the question of recent innovation or lack thereof.

7 Improving care for patients with CKD

Few patients with advanced CKD (GFR <45 mL/min/1.73 m^2) even know they have kidney disease.

Currently, there is not a systematic approach to population health for patients with CKD. Nephrologists and other providers should work together to develop new, improved approaches for care for patients with CKD.

8 Increasing access to kidney transplant

Most agree that transplant is the optimal therapy for patients with kidney failure. Yet few patients benefit from a transplant: only 2.6% of patients with kidney failure receive a preemptive transplant as a treatment; the remaining 97.4% start dialysis. Nephrologists and other providers should work together to develop new approaches to improve access to kidney transplantation.

9 Improving end-of-life care

Patients >80 years old with multiple co-morbidities have comparable outcomes if they receive comprehensive conservative care instead of dialysis, yet few choose this option. One of the barriers to improving access to non-dialytic care for those who might benefit more from an aggressive medical approach to their uremia, rather than from dialysis, is the lack of training in non-dialytic care. In addition, patients on dialysis at the end of life utilize hospice much less frequently than other patients with similar co-morbidities and cost of care. Nephrologists and other providers should work together to improve end-of-life care, both for patients with CKD and patients on dialysis. ASN could explore curricula elements that inform nephrology trainees about medical strategies that extend the duration and quality of life without dialysis.

10 Improving access to home dialysis

Most nephrologists and clinicians would choose home dialysis for themselves, yet few patients on dialysis are able to benefit from dialysis at home. A patient dialyzing at home has more autonomy, is more likely to continue to work, and has more satisfaction in their kidney care. Many training programs do not have a sufficiently large home dialysis program to adequately train fellows. They therefore have difficulty recognizing appropriate candidates for home modalities and do not feel comfortable prescribing home dialysis when they get into practice. Nephrologists and other providers should work together to identify opportunities to make it more likely that patients on dialysis can benefit from home dialysis, including rethinking curriculum structure and requirements for training and competence in home dialysis.

Allen R. Nissenson, MD, is CMO, DaVita Kidney Care; Franklin Maddux, MD, is CMO, FMC North America; Doug Johnson, MD, is CMO, Dialysis Clinics Inc.; Tom Parker, MD, is CMO-Emeritus, Renal Ventures Management; Brigitte Schiller, MD, is CMO, Satellite Healthcare.

ASN President: State of Kidney Care 2016

By Eleanor D. Lederer, MD, FASN, with David White

Medical care in the United States is poised to undergo one of the most comprehensive transformations in the past 50 years, prodded by ever-rising costs and poor population health performance. To address these and other challenges, Congress—with support from President Barack Obama—passed the Medicare Access and CHIP Reauthorization Act (MACRA) in 2015. MACRA has led to Medicare's creation of a new physician reimbursement system, the Quality Payment Program (QPP). QPP represents the most significant step to date in transitioning from a volume-based reimbursement system to a value-based one. Transitions of this magnitude engender anxiety among patients about legitimate concerns for their medical care and for providers who have equally legitimate concerns about their role in the new order. In my opinion, no group of health care providers is better equipped to comprehend and implement these changes than nephrologists.

For decades, nephrologists have worked within ever increasing regulations, guideline expectations, and cost-conserving measures. And they have succeeded in adjusting their practices accordingly while simultaneously delivering state-of-the-art care to the ever-growing population of patients with kidney diseases. Nephrologists have firsthand experience in the comprehensive care for patients with multiple co-morbidities over extended periods of time, providing care for patients with kidney diseases at all stages, treating and guiding patients who transition between multiple treatment modalities, and supporting patients who need end-of-life care. These transitions for patients with kidney disease can be fraught with uncertainties and risks and require a robust patient-nephrologist relationship. Nephrologists are uniquely positioned to assume leadership roles in the development and implementation of new, thoughtful health care delivery models. Yet, in order to accomplish these goals, nephrologists have to stand up and speak up. As US medical care undergoes transition, so will nephrology as a profession, nephrologists as a group, and the American Society of Nephrology (ASN)—as an advocate for patients and nephrology health professionals.

How positive this transition or transformation is may largely be determined by the role nephrologists play and the leadership nephrologists offer as a collective profession. In his ASN President's Address at ASN Kidney Week 2016 in Chicago, Raymond C. Harris, MD, FASN, eloquently outlined the path forward.

Surveying the crossroads

In the United States, interest in nephrology as a career has decreased among internal medicine residents. There are a host of factors behind that decrease. In my opinion, contributing to a softening of interest in the profession is increasing concern about issues of reimbursement and of career autonomy. The dominant role of dialysis in the practice of nephrology combined with the increasingly prominent role of the dialysis organizations in defining nephrology practice have led some to question whether the relationship between the dialysis organizations and nephrologists has become imbalanced.

Federal policy decisions further complicate the situation, such as the failure to implement laws allowing the provision of antirejection medications for the life of a kidney transplant or to protect the insurability and job security for living kidney donors. These policy decisions appear to be shortsighted and driven by short-term budget considerations rather than consideration of the best long-term results for our patients. The recertification process and the realities of practice feel misaligned to many. Research funding for kidney diseases by federal agencies and foundations has stagnated, diminished, or, in some cases, disappeared, dissuading young investigators from entering the field.

The current system of reimbursement for end stage renal disease (ESRD) care has led to the entrenchment of "silos" of kidney care, fragmenting the delivery of nephrology care to patients with chronic kidney diseases, ESRD patients on dialysis, and transplant patients. How the QPP might create new opportunities to overcome this situation may prove challenging as Medicare moves to a quality system emphasizing care coordination.

Determining the nephrologist's role in the practice of medicine

Despite the decline in nephrology fellowship applications, surveys indicate that the vast majority of nephrologists in practice enjoy their work and feel engaged. The same conclusion is borne out by nephrology trainees in those surveys, which suggest that defining the role of the nephrologist in comprehensive kidney care may provide a more attractive view of the profession and enhance recruitment. Nephrologists have long worked as members of multidisciplinary health care teams and have engaged providers at all levels—clinic managers, APRNs, PAs, nurses, dietitians, social workers, pharmacists—to provide the best care for patients with ESRD. Nephrologists need to actively define their role in the practice of medicine, and to occupy that space as leaders in care throughout their patients' journeys through stages of kidney disease.

Nephrologists should also look for leadership roles across the kidney care delivery spectrum. There will be a variety of settings for professional development where nephrologists can play a leadership role such as LDO chief medical officers (CMOs), SDO CMOs, hospital CMOs, and more.

A large kidney disease population with high rates of co-morbidities demands coordinated care. The nephrologist is an internist first and foremost and should not easily cede oversight care of their patients' non-kidney conditions. Under the incoming quality-based system with a heavy emphasis on clinical outcomes, it is important that nephrologists remain hands-on to ensure optimal outcomes.

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State of Kidney Care

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Working toward Comprehensive Kidney Disease Care

Patients with kidney diseases need comprehensive kidney disease care. Nephrologists should play a significant role in developing that model along with primary care physicians, transplant nephrologists and surgeons, pediatric nephrologists, dialysis organization CMOS, nurses, social workers, and regulatory agencies. A greater focus needs to be placed on guiding patients through transitions such as transitioning to late-stage kidney diseases, dialysis, transplantation, and back to dialysis.

If there is to be a re-imagined comprehensive kidney care approach that follows care across, and breaks down, silos, then there must also be a re-imagined role of the nephrologist who leads the team. There must also be a role for the primary care physician as well as transplant surgeons and nephrologists, medical directors and CMOs of dialysis organizations, nurses, social workers, and others to provide unified, seamless care. Medicare will continue to move toward value and clinical-based outcomes for reimbursement, and such an approach demands coordinated care.

As Dr. Harris said in his President's Address at Kidney Week 2016, now is the time to broaden, not constrict, the vision of what a nephrologist is. The logical conclusion follows that the nephrologist's role in the care continuum would broaden as well. The current training for nephrologists needs to also emphasize interventional techniques, novel imaging modalities, clinical genetics, and immunology. Perhaps all medical training should include medical economics and administration as well as international medicine and global health.

Making the case for aggressive funding for innovation, discovery, and research

Few parts of kidney care are more in need of a transition to a better state than funding for research and discovery. The investment in innovation, discovery, and research in kidney diseases must grow if the burden of kidney diseases is to be reduced. Kidney diseases affect 300 million people around the world, including more than 20 million Americans. More than 650,000 Americans have kidney failure and need dialysis or a transplant to live.

Kidney failure is unique in that it is the only health condition automatically covered by Medicare regardless of age or income, and the costs to the program are staggering. Medicare spends over $32 billion annually on the ESRD Program alone, which is 7% of Medicare's budget for less than 1% of its patient population and more than the entire budget for the National Institutes of Health (NIH).

To reduce the large Medicare commitment to the ESRD program, ASN has advocated that Congress must increase its commitment to curing kidney diseases by boosting funding for research. In addition to fully funding the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at NIH for Fiscal Year 2017 (October 1, 2016, to September 30, 2017), Congress needs to allocate an additional $150 million per year over 10 years for NIDDK-funded kidney research above the current funding level. These are crucial and necessary investments for preventing illness and maintaining fiscal responsibility. Investing in research to slow the progression of kidney diseases and improve therapies for patients would yield significant savings to Medicare in the long run.

A state of transition is here. Nephrologists, other health professionals, and ASN must work together with CMOs and other stakeholders—especially patients and their families—toward a future in kidney care that builds on the amazing advances of the last half century for continued advancements for patients, nephrologists, and the entire state of medicine.

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Fellows Corner

Dialysis Decision-Making: Can We Help Patients and Providers through the Process?

By Rob Rope

Millions of lives have been successfully prolonged through dialysis. However, the world of dialysis has changed since its inception. With time, our patient population has evolved from young and fit to old and sick. Belding Scribner, the father of chronic dialysis in the US, noted the need for a "deselection committee" just five years after the Medicare payment benefit for ESRD was established in response to his perception of the loosening of dialysis criteria (1). Notably, there is a growing body of literature indicating that dialysis does not meaningfully improve outcomes in many older and sicker patients, placing greater emphasis on dialysis decision-making in the outpatient setting (2,3). What are we to do in situations where dialysis may not be appropriate?

Ethically challenging situations rarely have a correct answer and it is important to remember that "death is as integral an aspect of human life as it is of all other biologic species."(4) In 2010, the Renal Physicians Association released updated guidelines to help providers and patients in dialysis decision-making (5). These can be downloaded free online and are worth reading. The guidelines give specific clinical instances where it is appropriate to either forgo dialysis outright, or consider forgoing (Table 1). The more common, and perhaps more challenging, cases tend to fall in the latter group.

Table 1
Renal Physicians Association guidelines on shared decision-making

Forgo Dialysis in Situations Where:	Consider Forgoing Dialysis in Situations Where:

• Patients, or surrogates, do not want dialysis.
• Patients have "irreversible, profound, neurological impairment such that they lack signs of thought, sensation, purposeful behavior, and awareness of self and environment."
	• Dialysis is unfeasible due to safety concerns (e.g., dementia, schizophrenia) or instability (e.g., hypotension)
	• Patients have a terminal illness aside from renal failure
	• Patients with advanced age (>75) with 2 or more of the following:
	  ○ Answer of "No" to the question "Would you be surprised if the patient died in the next 12 months?"
	  ○ High comorbidity score
	  ○ Impaired functional status (e.g., Karnofsky score <40)
	  ○ Chronic malnutrition (e.g., serum albumin <2.5 g/dL)

The goal of providing dialysis to extend life while also maintaining an acceptable quality of life is a reasonable starting point when assessing if dialysis is an appropriate therapy. This goal involves identifying what patients want and what providers can deliver. This forms the basis of shared decision-making. Commonly articulated goals of care include: cure, prolonging life, improving or maintaining quality of life, comfort, and providing support for others (6). Dialysis cannot deliver all of these at the best of times and sometimes cannot deliver any. Without understanding why a patient may want to extend their life through the toxicity of dialysis (including fatigue, hypotension, cramping, etc.), it is impossible to have an adequate conversation about the risks and benefits. Providers need to understand a patient's motivations, and patients need to understand what symptoms dialysis will help, as well as what may be worsened.

While medicine has embraced "shared decision-making" as standard-of-care, providers must not view this as avoiding paternalism at all costs. Imagine the last time you went to a mechanic. Although you did not want to be led astray into an expensive repair just to pad the shop's bottom line, you probably also did not want a list of options without any guidance as to what might be appropriate based on your budget, your car's mileage, or its sentimental value. In the name of doing the "right thing" and avoiding paternalism, nephrologists may defer to family or other health care providers regarding whether or not to initiate dialysis. This can contribute to provider and patient regret in retrospect. Unfortunately, some data indicate that patients often regret initiating dialysis and may start dialysis based upon family or provider wishes rather than their own (7).

How might these discussions and outcomes be improved for providers and patients? One potential approach to these discussions is outlined in Table 2. The October 2016 edition of *CJASN* also provides several articles outlining supportive care and other end-of-life issues. In addition, training programs, like NephroTalk, can improve provider preparation for dialysis decision-making conversations and should be incorporated into fellowship curricula (8). These programs should be made available to practicing providers for CME. Providers need to feel comfortable discussing and providing options aside from traditional dialysis, including conservative care and referrals to hospice, otherwise options may be presented as "dialysis or death." As death is usually not a primary goal for patients, dialysis may seem like the only option and conversations may be unproductive. Lastly, an increased focus on conservative care programs nationwide, as well as increased nephrology training in dialysis decision-making and symptom management, could increase resources for patients and providers when dialysis is not the appropriate choice.

Table 2
Potential approach to discussions about starting/stopping dialysis in the elderly (6)

Assess patients' goals of care and place their prognosis within this context. Initiate advance care planning including advanced care directives and potentially physician orders for life-sustaining treatment (POLST).

1) Discuss individualized treatment options and likely outcomes (best case/worst case) with patients and families.
2) Make treatment recommendations to fit a patient's goals of care if the patient/family prefers or struggles with decisions.
3) Consider recommending against dialysis in patients with poor prognosis, contraindications, or safety concerns.
4) Consider time-limited trials with predefined goals that are measurable, reasonable, and obtainable within a specific time period. Document goals to facilitate future discussions.
5) Identify and treat burdensome symptoms. Consider palliative care consultation in challenging cases.
6) Periodically reassess patient willingness to continue dialysis and facilitate discontinuation when consistent with goals of care.

Rob Rope, MD, is a third-year nephrology fellow at Stanford University.

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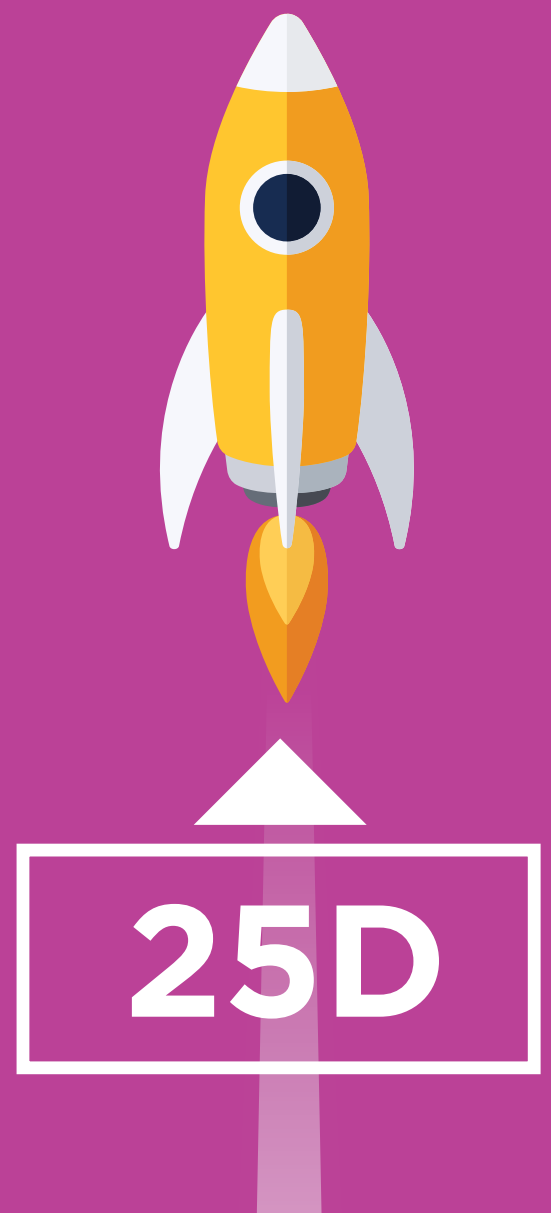

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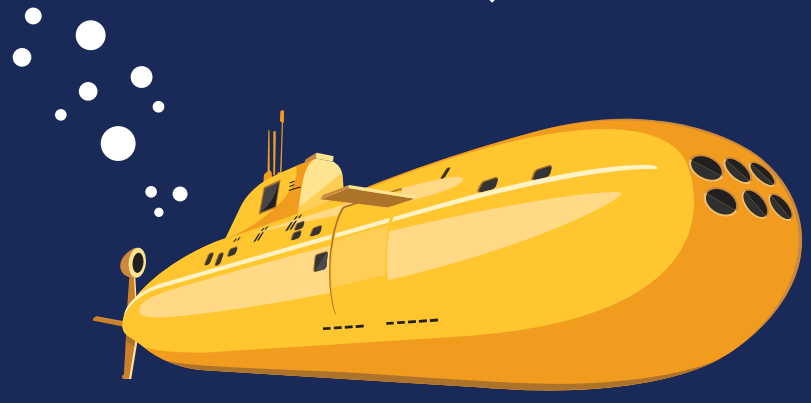

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American Kidney Care in a New Governance Landscape

By Richard Lafayette, MD

We cannot discuss too much or focus in too much detail on the issues when it comes to the historic transition of power and influence post-election. Much has been said about radically changing the government, and health care has been in the crosshairs throughout the election and in planning for transition. Governance and policy will be all important in 2017. Although there is limited detailed conversation about how change will occur, there surely will be new policy and rules.

The clearest promise has been that the Affordable Care Act (ACA) would be dismantled and fully repealed. Soon after the election, it appeared clear that not all of the ACA would be discarded, with continued coverage for children under their parents' policies until age 26 and likely extended coverage for preexisting conditions. However, how to ensure access to the millions of Americans covered under present ACA policies has not been clarified.

There have been broad statements about entitlements by the incoming congressional majority. What this will mean to Medicare, its coverage system (at what age, how costly the premiums, and how extensive the benefits will be), and whether Medicare will soon be allowed to negotiate pharmaceutical and device prices remain to be seen. How the federal government administers Medicaid programs will also be up for grabs, with discussions leaning toward allowing states to have even more responsibility and decision-making authority for running the programs for the financially most vulnerable part of our population. Block grants will limit federal exposure to rising costs but will likely limit benefits to those mired in poverty.

There have been few indications about the new administration's views about support for research and innovation, areas that bear watching in 2017. In a conversation last year, President Trump suggested NIH is a mess, yet he has also voiced his commitment to the nation's health and vowed to make American health care great again. We will see how this pushes policy toward the budget and priorities of the NIH, its intramural and extramural programs, and toward the support of industry initiatives to advance.

There has been little specific discussion of kidney health. Because ESRD care is mandated by the 1973 Social Security Act as a federal entitlement, it is not beyond the reach of change in the new leadership environment. Those not covered by Medicare often need help from Medicaid. Whether investments will be made to ensure the highest levels of care and to maintain the present focus on high-quality, cost-effective care is yet to be seen. Recent inroads into predialysis care that have blossomed with Medicare support may be revisited. Furthermore, new developments with payments of care through the Quality Payment Program legislated by MACRA may also be on the table for further revisions as the new administration makes its approaches to health care known.

As nephrologists, health care workers, and citizens of this country, we will need to work to stay at the table to let our opinions be known. I hope we can continue to move toward fairness and equity for our profession, for our patients, and for the diverse population that we care for. We must ensure that our nation maintains its commitment to access to health care, prevention of illness, and the most effective, sincere commitment to advancing knowledge in nephrology through continued support of education and research.

—Richard Lafayette, MD, Editor-in-Chief, ASN Kidney News

Likely Repeal of ACA Puts Coverage, Some Value-Based Initiatives in Limbo

The likely repeal of the Affordable Care Act (ACA) early in the Trump administration has placed patients who gained coverage through the legislation and the ACA's value-based kidney care initiatives in limbo.

The Trump administration and Republican leaders in Congress are vowing to quickly repeal the ACA when they take power in January 2017. The repeal is expected to allow a 2–3 year grace period for parts of the ACA to continue. After that time, Republicans are expected to replace the ACA with their own legislation.

The planned repeal raises many questions about what will happen to patients who gained coverage under the legislation, ACA programs for patients with kidney disease, and some of the patient protections in the bill.

Access to care

President Trump said shortly after the election that he would keep some protections, such as provisions that prevent individuals from being denied coverage based on preexisting conditions.

"From what I've seen, there seems to be a slight pulling back from a full repeal and all of its features," said Jeffrey Silberzweig, MD, chief medical officer at the Rogosin Institute. "I've always believed in a cautious approach to things, so I'm pleased to see that."

But John Sedor, MD, chair of the American Society of Nephrology's Public Policy Board and a nephrologist at MetroHealth System in Cleveland, is concerned that some of his patients who gained access to insurance through the ACA may lose it. He noted that the number of patients without insurance at the public hospital where he works dropped from about 16–18% before the ACA to about 4% after. Those most vulnerable to losing coverage are patients, particularly minority patients, who also have the greatest risk of advanced chronic kidney disease (CKD), he noted.

"For CKD patients, it could destabilize their insurance and reduce their access to care," he said.

Both President Trump and House Speaker Paul Ryan (R-WI) have proposed changing Medicaid into a block grant program, which they say would give states more flexibility in how they administer the program. These changes could mean that coverage under Medicaid would vary by state.

"I'm concerned about Medicaid block grants to states, which I think will allow more latitude and perhaps unintentionally block people from access to insurance products," Sedor said.

The effect of this change on health care providers would likely depend on which state they practice in, Silberzweig noted. For example, the Rogosin Institute is based in New York State, which has been generous in providing access and funding for the state's Medicaid program.

"It would have less of an impact [in states like New York], than in states that have not historically been as generous," he said.

Innovation projects

The United States has launched several efforts in the past 8 years to shift away from a fee-for-service payment model for physicians to value-based payments. The future of the Center for Medicare & Medicaid Innovation (CMMI), which administers many of these models, may hang in the balance as Republicans reshape health reform.

The 2015 MACRA legislation, which established a new system for Medicare payments for doctors that emphasizes value-based care, was passed by huge bipartisan majorities in both houses of Congress, noted Robert Doherty, senior vice president of policy and government affairs at the American College of Physicians, during a session on alternative payment models at Kidney Week 2016 in November. The MACRA legislation, which goes into effect this year, is unlikely to be changed under the new administration, he noted.

But the CMMI, which was created under the ACA and also has a role in MACRA, could be in jeopardy. The CMMI was created to test and fund various innovative payment and quality improvement programs, including the Comprehensive ESRD Care Model and the Medicare Shared Savings Program.

"Here's the one interface with ACA that has me concerned," Doherty said. "If Republicans deliver on repealing all of the [ACA], the innovation center would go away. Where would the funding come from for all the projects being supported by the [CMMI]?"

The CMMI has been unpopular with Republicans, noted Sedor. For example, more than 150 Republican congressmen and women sent a letter to Centers for Medicare & Medicaid Services administrators in September 2016 arguing that the CMMI had overstepped its authority in creating mandatory payment demonstration projects (http://bit.ly/2d1CDRY). Among those signing the letter was Sen. Tom Price, MD, (R-GA), and President Trump's nominee to head the Department of Health and Human Services.

It might be possible to create other mechanisms besides the CMMI to take over MACRA-related roles, Sedor said. "We're going to have to wait and see how things evolve when they take over," he said.

Organizations, like the Rogosin Institute, that are participating in the the Comprehensive ESRD Care Models and have invested heavily in infrastructure and staff for the projects are concerned about what will happen to their projects if CMMI disappears.

"It would be very difficult for us if they completely pulled funding for existing projects," Silberzweig said. "I think it would be fairer to continue funding existing projects at least for the demonstration period that was part of the original proposals and not fund new projects."

"My view is that we all need to proceed cautiously at this point until we get into [the new year] and the new administration steps in and does whatever they are going to do," Silberzweig said.

Sedor urged the administration and Congress to carefully consider the impact of any changes they make on people who are currently covered under the ACA.

"I'm a fan of the ACA," he said. "It certainly has issues that need to be addressed. But it was a game changer in terms of providing access to millions of people who were uninsured."

What Do Fellows Want? What Does Nephrology Need?

By Joseph Mattana, MD

After several years of declining interest, the future of nephrology as a career choice continues to be uncertain. Preliminary results from the Nephrology Match AY 2017 revealed a continuing trend toward unfilled nephrology tracks, with almost no change from AY 2016 (95 vs. 93 filled tracks). Programs may face the difficult choice of trying to recruit post-match or perhaps reducing program size and recruiting either more attending nephrologists or physician extenders including physician assistants or nurse practitioners.

Last year's match rate for nephrology was the lowest for all medicine fellowships. A particularly noteworthy trend has been the progressive decline in the number of international medical graduates (IMGs) matching in nephrology, with only 100 for the current academic year, down from 192 as recently as 2011.

As has been well described elsewhere, careers in nephrology have been viewed less favorably in recent years for a variety of reasons, including perceived lower compensation compared to many other fields along with a workload and quality of life felt to be inferior compared to other specialties. There is also concern regarding the ability to find nephrology jobs, with a large proportion of fellows describing difficulty finding positions in nephrology after graduation, as described in the 2015 Survey of Nephrology Fellows.

Need for innovations

Other factors may be playing a role as well. Dialysis and transplantation represent extraordinary therapeutic milestones that transformed end stage renal disease care, and these modalities have continued to improve. However, many fellows and trainees who are considering careers in nephrology are looking for new therapies comparable to what they see taking place in other fields. Trainees describe seeing many recent advances in cardiology, rheumatology, hematology/oncology, and endocrinology with new therapies regularly introduced. In contrast, for a number of renal conditions such as diabetic nephropathy, many note that there have been no major new therapies introduced in the past several decades with a string of disappointing clinical trials.

There are potent competing forces as well. Careers in hospital medicine appear to be a frequent alternative chosen by trainees considering nephrology careers. Better compensation, controlled schedules, and perceived better quality of life draw a number of residents away from nephrology. Whether such choices typically lead to long-term career satisfaction remains to be determined.

There have been some favorable trends whose impact will require observation over the next year. While the high percentage of fellows reporting difficulty in finding a satisfactory job as noted above is of great concern, this percent-

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What do Fellows Want?

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age has recently fallen, mostly for US medical graduates, but to some extent for IMGs as well. If this trend continues, we might see a positive impact on the perception of nephrology by residents considering it as a career and hopefully greater career choice satisfaction for nephrology fellows.

Nephrologists' role in emerging health care

At the same time that changes in the nephrology workforce and in what fellows want are taking place, several variables are affecting the emerging needs of nephrology. There has been a decline in the incidence of ESRD, likely in part due to more aggressive treatment to slow progression of CKD. Nephrologists will need to continue to be a part of this effort if this trend is to continue. Despite a decrease in incidence, the prevalence of ESRD has increased, due to factors such as the growth of the population, with a large percentage having diabetes mellitus and hypertension, and improved dialysis care leading to a reduction in mortality. Nephrologists will obviously be essential to their care, even as the role of physician assistants and nurse practitioners continues to evolve.

Kidney transplantation has seen the introduction of new agents such as belatacept that require additional expertise on the part of nephrologists. Hence a larger number of nephrologists who are highly competent and comfortable in the use of such therapies may be needed. The nephrology workforce, as for many other physician specialties, tends to be unevenly distributed across the country, with some areas having high concentrations of nephrologists and others with a severe shortage and large obstacles to recruitment. Challenges with recruitment to certain areas could potentially be addressed through telemedicine, for example in areas with large distances between dialysis units.

A further area of uncertainty that will affect the needs of nephrology will be the impact of emerging models of health care including the roles of physician extenders. For example, as described in the US Adult Nephrology Workforce 2016 Report, the ESRD Seamless Care Organization (ESCO) will be one such model whose potential impact cannot be determined at this time in terms of the job market for nephrologists. Whether through an ESCO or other model, increased use of physician assistants and nurse practitioners is a phenomenon whose impact on future career opportunities for nephrologists merits close watching.

Nephrology has made enormous advances but is in need of much more progress to ensure the ability to draw fellows who will pursue careers in clinical practice as well as those with potential for careers as nephrology researchers and educators. The excitement and vast potential of nephrology research, the deep personal rewards that come from caring for patients with renal disease, and the satisfaction derived from mastery of the subject matter of nephrology while maintaining a strong command of general internal medicine all need to be communicated to students and residents. Novel elective models and other interventions to expose students and residents to a broader spectrum of nephrology have been proposed and are being utilized at various institutions, with impacts that deserve further study. It is hoped that over the coming year we will start to see some reversal in the recent trend away from pursuing careers in nephrology and gain further insights in how to facilitate this.

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The Nephrology Care Team: Whose Responsibility is it to Educate?

By Amy Williams, MD

Leaving ASN Kidney Week 2016, I was excited to integrate new knowledge and thoughts into processes to improve the care and outcomes of patients with advanced CKD. Realizing that outcomes for these patients depend on early identification and appropriate management throughout their disease trajectory with attention to transitions across settings of care, and during disease progression or additions of co-morbidities, begs the question: Whose responsibility is it to bring up-to-date knowledge to the community primary care practitioners, home health agencies, other subspecialists, and anyone else who participates in the care of those with CKD 4+?

A critical first step in answering this question is defining who is on the extended care team and what role each team member plays. Certainly the team's anchor is the patient, but the captain or general manager must be the one with the most knowledge related to managing the patient population. For CKD and particularly CKD 4+, it is the nephrologist.

Patients have told us that to gain maximum usability of information, they want timely, transparent, open, and honest conversations that contain information with a tight feedback loop translated on their level and relevant to their current disease state. They also ask that all members of their care team have and share the same information to avoid confusion. Whose responsibility is it to manage the information? It is the nephrologist's.

With crammed office schedules and many competing responsibilities, the nephrologist does not have the luxury of spending the time needed with each patient to adequately educate them on their disease and treatment options, including conservative care. Reliable processes are needed to monitor disease progression, co-morbidities, and treatment effectiveness. Without effective and efficient processes, patient safety and outcomes are at risk. Health care delivery systems with multidisciplinary teams educated about the target population and disease cluster, captained by the content expert provider, can mitigate these risks.

Patients want a continuous connection to their medical care team, but only want a face-to-face meeting when necessary. Education theory tells us that the most effective learning method is iterative with repeated discussions and teach-back. A 15-minute office visit with the nephrologist will not accomplish this goal. In fact, the time the nephrologist has with the patient is critically valuable—and should focus on discussions and complex decisions that only the nephrologist is trained to do.

Care teams should be designed to easily share knowledge across settings, accomplishing this through web-based care algorithms and links to educational materials.

Also, it is not patient-centric to interrupt patients' lives for an office visit if the assessment and care decision can be made virtually through synchronous, live, two-way video interactions between the patient and care team member—RN, advanced practice provider (APP), dietician, social worker, pharmacist, and if needed, the nephrologist, using audiovisual telecommunication technology. Review of health records or lab data via asynchronous transmission to the nephrologist—possibly reviewed and triaged by a trained RN or APP with knowledge and algorithms to determine whether the patient should be seen in the office or not—can be effective and efficient. Managing ESRD patients either at home or in-center is also best when team-based. We are accustomed to employing a team-based model in dialysis units, depending on the social worker and dietician to fill in our skill and knowledge gaps, or nurses to lead just-in-time educational sessions with patients. These models should be expanded to pre-ESRD care models.

It is important to include other providers who care for the advanced CKD patient on the team. Shared care plans, knowledge of best practices and electronic health records, as well as establishing easy referrals using face-to-face office visits or virtual evaluations are important steps to smooth care and disease transitions resulting in improved outcomes for this complex patient population.

As the CKD population increases and decisions for patients with complex chronic disease become more complicated, it is imperative that nephrologists stay in the captain or general management role, leading the care team by sharing their knowledge and expertise and giving timely input. Success depends on staying connected to patients in a way that supports them when they need support. Care teams should be designed to easily share knowledge across settings, accomplishing this through web-based care algorithms and links to educational materials. The key is to have the resources available to the providers and care team members when they need it—at the bedside or in the office.

In summary, to accomplish population management in the CKD 4+ complex chronic disease population, nephrologists must develop expanded care teams that include flexible partnerships with other providers and the community. Their responsibility as general manager or captain includes coordinating consistent integrated flow of information, and developing an expanded CKD/ESRD team with standardization of care and of care team members' roles—including the patient. Accomplishing this should lead to the goal of improved outcomes through effective management of kidney disease and the co-morbid conditions common in patients with advanced kidney disease.

Amy Williams, MD, is Associate Professor of Medicine in the Mayo Clinic School of Medicine and consultant in the Division of Hypertension and Nephrology. Dr. Williams is a member of the Kidney News *Editorial Board.*

Findings

High Rates of AKI in Pediatric ICUs

Acute kidney injury (AKI), often severe, develops in more than one-fourth of children admitted to pediatric intensive care units, reports a study in *The New England Journal of Medicine*.

The prospective study included data on patients (aged 3 months to 25 years) admitted to 32 pediatric ICUs worldwide over a 3-month period in 2014. Based on Kidney Disease: Improving Global Outcomes criteria, stage 2 or 3 AKI occurring within the first 7 days in the ICU was classified as severe. Increases in morbidity and mortality associated with AKI were assessed as well.

Stage 1 or higher AKI developed in 26.9% of patients, while 11.6% met criteria for severe AKI. Mortality within 28 days was 11.0% in patients with severe AKI, compared to 2.5% in those without severe AKI: adjusted odds ratio 1.77. Patients with severe AKI were also more likely to require mechanical ventilation and renal replacement therapy.

Mortality increased in stepwise fashion with the maximum stage of AKI. Assessing AKI based on plasma creatinine alone missed the diagnosis of AKI in 67.2% of patients with low urine output. The prevalence of AKI increased from 14.5% on ICU day 1 to 20.4% on day 7.

The data show the high rate and clinical impact of AKI in pediatric ICU settings. Severe AKI is associated with an increased risk of adverse outcomes, prolonged ICU stay, and death. In contrast to the confounding effect of chronic diseases in adults, AKI in children may be a key contributor to increased morbidity and mortality [Kaddourah A, et al. Epidemiology of acute kidney injury in critically ill children and young adults. *N Engl J Med* 2016; DOI: 10.1056/NEJMoa1611391].

Differences in "Early" and "Late" ESRD in Live Kidney Donors

Patterns of end stage renal disease (ESRD) among live kidney donors may differ for those with ESRD developing earlier versus later in the postdonation period, suggests a study in the *American Journal of Transplantation*.

The researchers analyzed more than 125,000 US live kidney donors who underwent donor nephrectomy between 1987 and 2014, drawn from the Scientific Registry of Transplant Recipients. Median follow-up was 11 years; 59% of donors underwent nephrectomy between 1987 and 2005. Cause-specific cumulative incidence of ESRD due to diabetes, hypertension, and glomerulonephritis was analyzed for each successive postdonation year.

Over approximately 1.3 million person-years of follow-up, 257 donors developed ESRD. In 61% of patients, the cause was diabetes (33 cases), hypertension (70 cases), or glomerulonephritis (55 cases). Cumulative incidence of ESRD was 10 events per 10,000 donors per year at 10 years after donation versus 85 per 10,000 at 25 years. After adjustment for age, sex, and race, the incidence rate ratio for late versus early ESRD was 1.77.

Glomerulonephritis predominated as the cause of early postdonation ESRD, but diabetes and hypertension were more frequent in the late postdonation period: IRR 7.7 and 2.6, respectively. There was no significant time-dependent pattern for glomerulonephritis-related ESRD.

Studies of ESRD in live kidney donors have typically averaged less than 10 years' follow-up. The new findings highlight the need for caution in extrapolating these findings over longer periods. The increases in ESRD due to diabetes and hypertension underscore the importance of close monitoring of blood glucose and renal function, continuing for decades after nephrectomy [Anjum S, et al. Patterns of end-stage renal disease caused by diabetes, hypertension, and glomerulonephritis in live kidney donors. *Am J Transpl* 2016; 16:3540–3547].

Exercise Linked to Improved Metabolic Health in CKD

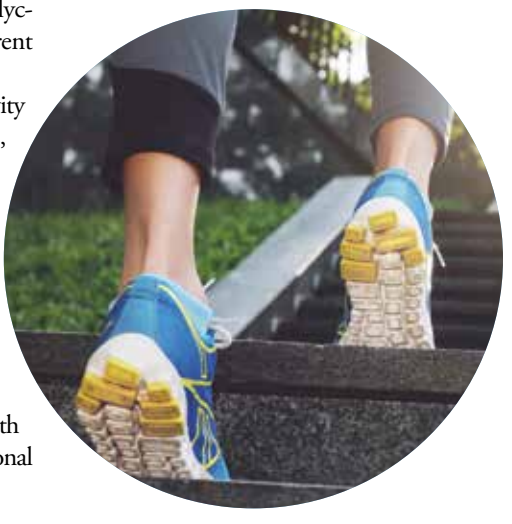
Among patients with moderate to severe chronic kidney disease, several measures of metabolic health are better in those with higher physical activity, reports a study in *BMC Nephrology*.

The cross-sectional study included 47 patients with CKD, mean estimated glomerular filtration rate (eGFR) 38.7 mL/min/1.73 m^2, and 29 controls with normal kidney function. All wore an accelerometer for 7 days to assess physical activity level. Associations between insulin sensitivity and metabolic parameters were assessed, including fat mass, blood pressure, lipid levels, and high-sensitivity C-reactive protein.

The CKD patients had lower physical activity than controls: mean 468 versus 662 counts per minute. The CKD group also had lower insulin sensitivity, 4.1 versus 5.2 mg/min; higher fat mass, 32.0 versus 29.4 kg; and higher triglyceride levels, 153.2 versus 99.6 mg/dL.

After adjustment for demographic and medical factors, including eGFR, CKD patients who were more physically active had more favorable levels of some metabolic measures. For each twofold increase in physical activity level, insulin sensitivity increased by 0.9 mg/min, fat mass decreased by 8.0 kg, and triglyceride level decreased by 37.9 mg/dL. Associations of physical activity with insulin sensitivity and triglyceride level were not significantly different between the CKD and control groups.

Interventions to increase physical activity might improve clinical outcomes in CKD, but little is known about the metabolic pathways of this benefit. This study shows that CKD patients who are more active have increased insulin sensitivity, decreased adiposity, and lower triglycerides. The findings may inform further studies of physical activity to promote metabolic health in CKD [Bowlby W, et al. Physical activity and metabolic health in chronic kidney disease: a cross-sectional study. *BMC Nephrol* 2016; 17:187].



High Racial/Ethnic Variation in ESRD Risk

Risk of end stage renal disease (ESRD) shows more than twofold variation across different racial/ethnic groups, according to a paper in the *American Journal of Kidney Diseases*.

The researchers analyzed USRDS data to estimate the short- and long-term probabilities (risks) of ESRD by age, sex, and race/ethnicity. Based on 2013 data, the lifetime risks of ESRD among males varied substantially by racial/ethnic group: 3.1% for non-Hispanic whites, 3.8% for Native Americans, 5.1% for Asian/Pacific Islanders, 6.2% for Hispanics, and 8.0% for non-Hispanic blacks. Lifetime risks were lower but also variable among females: 2.0% for non-Hispanic whites, 3.6% for Native Americans, 3.8% for Asian/Pacific Islanders, 4.3% for Hispanics, and 6.8% for non-Hispanic blacks.

From 2000 to 2013, the lifetime risk of ESRD increased from 3.0% to 4.0% in males and decreased from 3.0% to 2.8% in females. The disparity in lifetime ESRD risk for males versus females widened during this period: from about 1.2 in 2000 to 1.4 in 2013.

The USRDS routinely reports incidence rates of ESRD, but not the risk of developing this disease. This study shows substantial variation in the lifetime risk of ESRD: from a low of 2% for white females to more than 8% for black males. The authors note that information on additional ESRD risk factors will be needed to inform clinical practice and policy planning [Albertus P, et al. Risk of ESRD in the United States. *Am J Kidney Dis* 2016; 68:862–872].

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Practice Pointers

IgA Nephropathy

By Rosanna Coppo and Jürgen Floege

One disease or many?

IgA nephropathy (IgAN) is well identified by dominant IgA glomerular deposits; however, this immunohistologic entity can be an asymptomatic chance finding or present with an extremely variable course. The variable clinical and histologic expressions are likely to be the result of genetic and environmental factors modulating common pathogenetic and progression mechanisms.

Who gets IgAN, and what do we know about the origins?

There is genetic heterogeneity, and no causal mutation has been detected. IgAN has genetically complex traits, and genome-wide association studies have identified susceptibility variants that are responsible for 6% to 8% of disease risk (1). Genome-wide association studies have indicated the involvement of pathways, including antigen presentation, complement activation, regulation of IgA mucosal synthesis, and innate immunity. These findings suggest a role for mucosal infections and intestinal immunity. The pathogenesis of IgAN is thought to develop on the basis of a genetic predisposition, only partially known, via multiple hits (2). The first hit is an abnormal production of galactose-deficient IgA1, which needs a second hit, represented by the production of autoantibodies directed against galactose-deficient IgA1, followed by the third hit, the formation of immune complexes in circulation. The deposition of complexes in circulation in the mesangium activates complement and other mediators, leading to inflammation and finally ending in fibrosis, which is the fourth hit.

How do patients present?

The clinical presentation can be apparently benign, with isolated microscopic hematuria or bouts of gross hematuria coincident with mucosal infections. The patients presenting these features are often young, with normal GFR and normal blood pressure (BP), and spontaneous remission can occur, particularly in children. On the contrary, in several patients, years after unnoticed microscopic hematuria, proteinuria develops, mostly around 1 to 2 g/d. These patients often present with hypertension and mildly reduced GFR. The diagnosis of IgAN can be missed if a renal biopsy is not performed, and some patients enter dialysis and transplantation programs without the recognition of the causal renal disease.

Who is likely to have progressive disease?

The detection, at renal biopsy, of proteinuria, hypertension, and reduced GFR is associated with potential progression (Table 1). However, the most significant risk factor for progression of IgAN is persistent (time-averaged) proteinuria (>1 g/d) and persistent hypertension. Also, mild time-averaged proteinuria (>0.5 to <0.9 g/d) has been associated with progression, indicating the need for renal biopsy and diagnosis of IgAN before the development of heavy proteinuria (3). Time-averaged proteinuria and mean BP over 2 years are predictive of outcome, but clinical decisions are usually taken at biopsy. The added value for individual prognostication of histologic features has been proven by the Oxford Classification of IgAN (4), indicating that the mesangial (M) or endocapillary hypercellularity, segmental glomerulosclerosis, and tubular atrophy/interstitial fibrosis lesions predicted renal outcome independent of clinical data at renal biopsy and during follow-up. Addition of M or endocapillary hypercellularity, segmental glomerulosclerosis, and tubular atrophy/interstitial fibrosis lesions to baseline GFR, proteinuria, and mean BP improved prediction of patient risk, with accuracy comparable with the 2-year follow-up data (5). Patients with M1 are at risk, even if proteinuria at biopsy is <1 g/d, whereas those with M0 and tubular atrophy/interstitial fibrosis lesions 0 have low risk, even if proteinuria is 1 to 1.5 g/d (Table 1).

Supportive therapy: One for all and what does it include?

Given the usually long course of disease until renal failure develops, nonspecific measures that retard progression are key in the treatment of IgAN patients at risk for progressive loss of renal function. In sum, such measures are referred to as supportive therapy. Key components are the administration of renin-angiotensin system (RAS) blockers (i.e., ACE inhibitors or angiotensin receptor blockers uptitrated to achieve both sitting BPs in the 120s as well as a proteinuria below 1 g/d) (6). Both targets seem of equal importance. Nondihydropyridine calcium antagonists should not be used as first-line agents given their induction of glomerular hypertension. Other important measures are lifestyle changes (in particular, the initiation of a moderate protein diet; 0.8 g protein per 1 kg body wt per day, particularly if GFR is below 60 mL/min), salt restriction, nicotine abstinence, and treating all components of the metabolic syndrome (Table 2). In patients with proteinuria that was initially controlled by these measures but subsequently started to increase again, aldosterone breakthrough may have occurred. In such patients, a low dose of an aldosterone antagonist (e.g., spironolactone at 25 mg/d) may effectively reduce proteinuria again; if this approach is used, hyperkalemia is a risk, necessitating frequent monitoring and/or the addition of a loop diuretic.

Who should receive immunosuppression, and if so, which one?

Immunosuppression should only be considered in patients at risk for progression of IgAN (see above). There is relative consensus not to offer immunosuppression to patients with a GFR below 30 mL/min at baseline, unless one of the very rare rapidly progressive courses with widespread crescents and glomerular necrosis is present (7). Importantly, the detection of a single crescent in an otherwise stable clinical setting does not warrant immunosuppression but should rather call for RAS blockade. Immunosuppression has mostly relied on systemic corticosteroids, whereas combination therapy, mycophenolate mofetil, and calcineurin inhibitors are discouraged (7). A landmark trial in 1999 (8) as well as some subsequent trials showed that a 6-month course of initially high-dose corticosteroids with tapering can stabilize the course of disease. This trial and the subsequent trials, however, suffered from inconsistent RAS blockade or the requirement to halt RAS blockers before randomization (6). In our recent STOP-IgAN Trial, a 6-month-long optimization of supportive measures reduced GFR loss so much that no added benefit of immunosup-

Findings

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"Diabetes-Specific Experience" Linked to Quality of Diabetes Care

The quality of primary care management of diabetes is lower for physicians with higher-volume practices, but higher for those with greater diabetes-specific volume, reports a study in *Annals of Internal Medicine*.

Using Ontario health databases, the researchers analyzed data on more than 1 million adults with diabetes who received care from approximately 9000 primary care physicians during 2011. For each physician, overall ambulatory volume and diabetes-specific volume were assessed. These two measures were analyzed for association with six selected indicators of quality of diabetes care, addressing disease monitoring, prescription of appropriate medications, and adverse clinical outcomes.

For most indicators, overall ambulatory volume was inversely related to quality of diabetes care. The trend did not reach significance for adverse clinical outcomes (emergency department visits for hypoglycemia or hyperglycemia).

In contrast, diabetes-specific volume was directly related to quality of diabetes care," the researchers write. This was so for all six indicators studied. The associations were independent of each other and were unaffected by cardiovascular disease status or socioeconomic factors.

Little is known about whether physician volume affects the outcomes of outpatient care for diabetes or other chronic diseases. The new analysis suggests that primary care doctors with an overall higher patient volume deliver lower-quality diabetes care.

The results also show that physicians with greater diabetes-specific experience deliver consistently better diabetes care, including lower rates of adverse clinical outcomes. "Health policies or programs to support physicians with low volume of patients with diabetes may improve care," according to the authors [Cheung A, et al. Primary care physician volume and quality of diabetes care: a population-based cohort study. *Ann Intern Med* 2016; DOI: 10.7326/M16-1056].

pression on the course of GFR could be detected (9). An effect of immunosuppression on inducing full clinical remission was noted in some patients with a baseline GFR above 60 mL/min, but this benefit was offset by a 50% increase in infections and significantly more diabetes induction and weight gain (10). Thus, at present, systemic corticosteroids should be used restrictively in high-risk IgAN patients, only be considered after optimization of supportive measures, and probably be reserved for those patients who still exhibit a proteinuria above 2 to 3 g/d despite these measures.

What novel therapies are on the horizon?

Given the uncertainty of the value of systemic immunosuppression in IgAN and our increasing knowledge on the pathogenesis of IgAN, alternative approaches are of great interest. On the basis of a small pilot trial (10), the NEFIGAN Phase II Trial recently evaluated effects of budesonide encapsulated to achieve preferential release in the terminal ileum in high-risk IgAN patients. In data presented at ASN Kidney Week 2015, this approach reduced proteinuria and stabilized GFR in the patients. A phase III trial is currently in the planning phase.

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Table 1
Risk factors for progression of IgA nephropathy: Importance as judged by an arbitrary score (0 to +++)

- Clinical data at renal biopsy: reduced GFR (+++), proteinuria >1 g/d (++), hypertension (++)
- Renal biopsy histologic features: MEST score: mesangial hypercellularity (++), endocapillary hypercellularity (±), segmental glomerulosclerosis (+), and tubular atrophy/interstitial fibrosis (+++)
- Crescents affecting >50% of glomeruli (uncontrolled data)
- GFR at renal biopsy considered together with follow-up (time-averaged) proteinuria and time-averaged mean arterial BP over 2 years (+++; see text for explanation)

Abbreviation: MEST = mesangial or endocapillary hypercellularity, segmental glomerulosclerosis, and tubular atrophy/interstitial fibrosis lesions.

Table 2
Supportive measures in IgA nephropathy patients at risk for progressive disease

- Control each component of the metabolic syndrome
- Restrict NaCl intake/institute diuretic therapy
- Nondihydropyridine calcium channel blocker therapy
- Aldosterone antagonist therapy (adapt dose to CKD stage)
- β-Blocker therapy
- Smoking cessation
- Allopurinol therapy (controversial)
- Empiric $NaHCO_3$ therapy independent of whether metabolic acidosis is present (controversial)
- Avoid NSAIDs if possible (if not, use maximally once or twice weekly)

Abbreviations: CKD = chronic kidney disease; NSAID = nonsteroidal anti-inflammatory drug. Modified from Floege and Feehally (6).

Kidney Disease Markers Reflect Heart Failure Risk in African Americans

Data on kidney function and microalbuminuria are associated with the risk of congestive heart failure in an African American population, reports a study in *Nephrology Dialysis Transplantation*.

The researchers present data from 3332 African American participants enrolled in the community-based Jackson Heart Study. All were initially free of heart failure. Baseline measurements showed that 5% of participants had an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m^2, while 12% had a urine albumin:creatinine ratio (ACR) of 30 mg/g or higher. These kidney disease measures were evaluated for association with later subclinical evidence (based on echocardiography) or clinically assessed heart failure.

In adjusted models, both measures of kidney disease were associated with increased left ventricular mass (LVM): β-coefficient 1.54 per 10 mL/min/1.73 m^2 decrease in eGFR and 2.87 per doubling of urine ACR. Neither measure was significantly associated with left ventricular ejection fraction.

The eGFR was unrelated to the risk of incident heart failure. However, urine ACR was related to clinical heart failure: hazard ratio 2.22 per doubling of urine ACR. This association was only slightly weakened by adjustment for left ventricular mass.

African American and other patients with chronic kidney disease are at high risk of heart failure. This study shows that eGFR and urine ACR are associated with increased LVM in an African American population. Urine ACR is associated with the development of clinical heart failure, even after adjustment for LVM. The mechanisms of these associations remain to be clarified [Bansal N, et al. Markers of kidney disease and risk of subclinical and clinical heart failure in African Americans: the Jackson Heart Study. *Nephrol Dial Transpl* 2016; 31:2057–2064].

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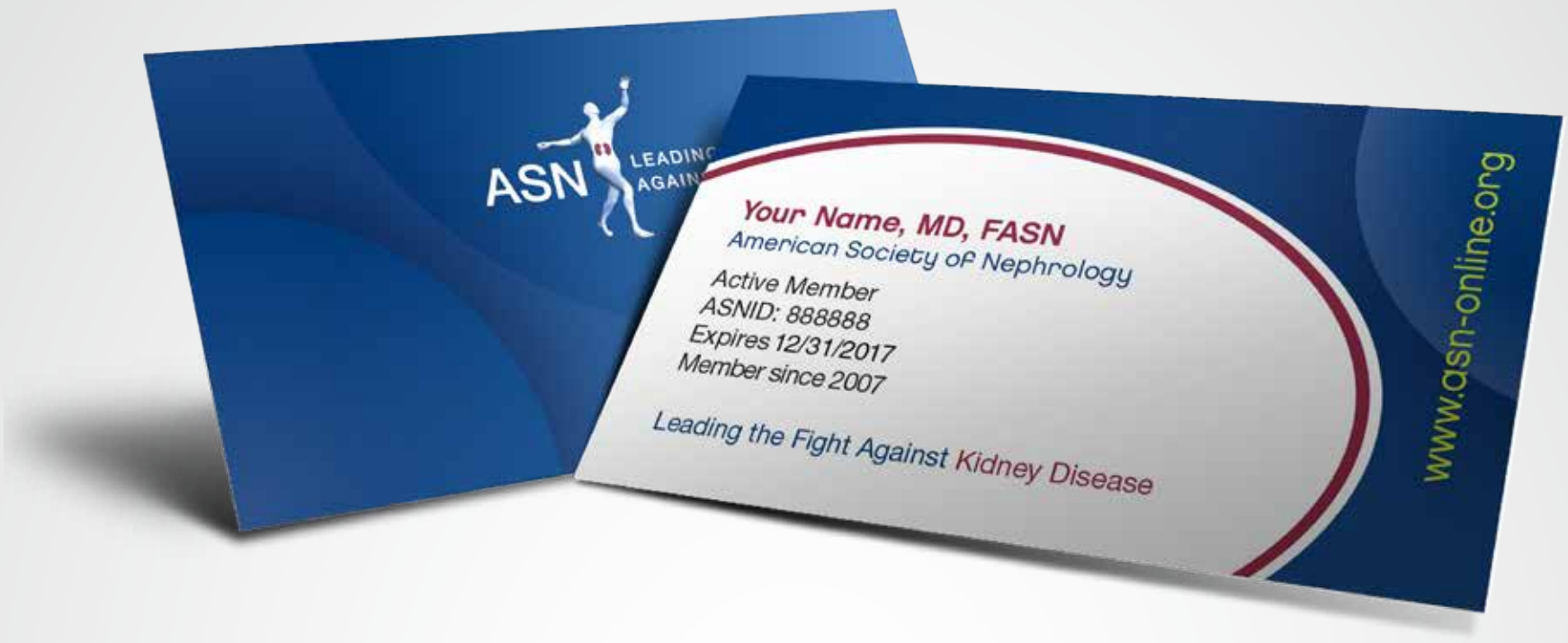

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Industry Spotlight

Possible Kidney Cancer Treatment; Alpha Blockers in Kidney Stones

Recent news of a new kidney cancer treatment in early studies and insight into when to use alpha blockers to treat kidney stones top recent industry developments.

A new kidney cancer investigational medication has had good results in a phase 1 study. The compound CB-839, developed by Calithera Biosciences in South San Francisco, targets glutaminase, an enzyme involved in the conversion of glutamine to glutamate, a nutrient that cancer cells need to survive, the researchers noted. "Glutaminase is a very interesting target, and previous work in the lab has shown that CB-839 is effective at inhibiting it in renal cell cancers and that it enhances the anti-tumor efficacy of everolimus (another renal cell cancer drug)," said Funda Meric-Bernstam, MD, chair of the department of investigational cancer therapeutics at the University of Texas MD Anderson Cancer Center in Houston.

In the 15-patient study, all but one of the patients with clear cell and papillary renal cell cancers exhibited tumor control from the regimen, with a median time without cancer growth of 8.5 months, Meric-Bernstam reported in a news release from the European Organisation for Research and Treatment of Cancer. Calithera Biosciences funded the study.

In other news, a review of the medical literature suggests when to use alpha blockers such as tamsulosin (Flomax) to treat kidney stones, according to a report in *The BMJ*.

First author John M. Hollingsworth, MD, associate professor of urology at the University of Michigan Medical School, and his team evaluated a total of 55 randomized controlled trials comparing alpha blockers to placebo or control. They also considered stone size and location in the 5990 study participants, to determine if either was a predominant factor for successfully passing a stone.

They found a 57% higher chance of stone passage for larger stones with an alpha blocker, but no benefit for smaller stones. Location and type of alpha blocker did not make a difference, the researchers noted.

"If we can facilitate kidney stone passage without surgery, it allows our patients to avoid extra pain and risks that come with a surgical procedure," Hollingsworth said.

"It's important not to discount low-risk options for patients who may benefit from them," said senior author Philipp Dahm, MD, professor of urology at the University of Minnesota Medical School.

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