Moving Nephrology Care and Caregivers FORWARD

By Richard A. Lafayette

As I considered possible developments in nephrology for this coming year, I could not help but think a bit further forward to the year 2020. This led me to think more about the Centers for Disease Control and Prevention's Healthy People 2020 initiative (1), the national blueprint designed to bring about effective preventive care and improved health to the U.S. population by 2020. This ongoing initiative started decades ago, issuing 10-year plans and starting with general interventions such as ensuring a clean environment, drinkable water, good nutrition, increased exercise, and access to high-quality healthcare. The plan then moved into care for specialty areas, including acute and chronic kidney disease (CKD).

One objective of Healthy People 2010—to reduce new cases of ESRD—was retained "as is" for 2020. Others were modified, and several new objectives were added. Overall, these objectives seek to reduce the incidence of ESRD, improve the mortality rates of incident and prevalent patients receiving dialysis, improve access to and outcomes of kidney transplantation, improve the identification and care of patients with acute kidney injury (including setting standards for follow-up), include specific objectives for patients with diabetic kidney disease (reducing rates, controlling BP and lipids), and finally improve the overall awareness of patients with CKD. As an example of goal setting, Healthy People 2020 determined that fewer than 10% of adults with CKD knew they had CKD. A stated goal was to increase awareness to 13.4%.

It is always interesting to see whether and how these objectives are fulfilled years after their introduction. The objectives of Healthy People 2020 are supported by funding from the National Institutes of Health (NIH) and other government research organizations and shaped by the Centers for Medicare & Medicaid Services (CMS), which creates incentives and penalties for providers to induce them to embrace and, it is hoped, achieve these goals.

In general, it is difficult to assess how successful these programs are in changing the nation's healthcare practices because data emerge slowly and outcomes may change through other actions. Clearly, the NIH and the CMS influence physicians' and providers' practices. Incentives and penalties do get attention and results, but often they risk corresponding changes in areas that are not under immediate focus (2). For example, if dialysis access becomes a focus for measurement and intervention, sometimes areas such as bone disease may get less attention. Large numbers of studies demonstrate that guidelines are often ineffective or take a long time to affect practice (3). Nonetheless, there is inherent value in experts gathering and setting goals for general health issues of the nation and for specific health conditions, such as those facing patients in nephrology practices. Often, just identifying focus areas allows increased attention, which can yield improved outcomes.

In the latter part of this decade, however, many strong influences have had an impact on the ability of physicians and other caregivers to provide optimal care. This both generally and specifically applies to nephrology. Nationally, payment reform has taken a lot of attention and time to try to learn, and it is still unclear whether caregivers will need to work harder and longer to earn the same incomes under pay-for-performance or risky cost-sharing schemes. Electronic medical records are increasingly prevalent and require huge chunks of time in logging in and out and in providing the appropriate documentation and services. They have generally shifted more and more work to the provider rather than to support staff. With regard to maintenance of certification, physicians continue to struggle to find the right balance between ensuring community standards for knowledge and diverting provider care toward efforts that do not improve care or efficiency.

More specifically to nephrologists, care in dialysis units is increasingly deter-

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mined by dialysis unit policies rather than by discussions between caregiver and patient, based on the bundle and requirements for frequent visits. Care in the hospital can be increasingly fragmented as hospitalists struggle to learn the stories of patients whom they don't care for as outpatients and as other specialists take on procedures traditionally done by nephrologists, such as biopsies, intravenous lines, and even continuous dialysis. The complexity of care of our patients seems to be ever increasing. These challenges threaten to lead to burnout and frustration, and they threaten to make the field one in which it is increasingly difficult to sustain a career. This also makes it harder to recruit future trainees.

The years 2019 and 2020 may usher in a further realization of these trends, and reform may become the new buzzword. Programs like Healthy People 2020 may actually show how nephrologists routinely improve patient care and add value to medical care, ultimately providing them a better bargaining position (4). Such programs may position nephrologists again to determine what procedures they do for their patients.

Long-promised innovations in electronic medical records may free up time for more effective face-to-face interactions and allow us to actually think about optimal care. Translational advances in dialysis, transplantation, acute kidney injury, hypertension, and glomerular disease (among others) may make nephrology ever more exciting as a field, ushering in greater joy in the profession and turning the tide on recruitment concerns.

Let's not just watch and see; let's try to make it happen.

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New Insights into Acute Kidney Injury and the Role of the Microbiome

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The gut microbiome is believed to have evolved with time and exists in symbiosis with the system in the healthy state because of its synthetic, metabolic, and immune properties. Recent studies have hypothesized that specific microbial metabolites, particularly short-chain fatty acids and D-amino acids (D-AAs), are important contributors to the maintenance of health. Disturbance of this relationship, known as dysbiosis, has been implicated in various diseases.

The emerging literature on the metabolic potential of gut microflora and its integral role in the pathogenesis of inflammatory conditions is attracting increasing interest from the nephrology community in further exploration of the gut–renal axis. For example, there is evidence that the microbiome may play a role both in the progression of chronic kidney disease (CKD) and in the uremic complications of CKD. In addition to CKD and complications of uremia, accumulating data suggest that the microbiome also plays an important role in the mediation of renal damage in acute kidney injury (AKI) (1).

Although the kidneys are generally not considered to be conventional immune organs, resident dendritic cells and macrophages play a role in the maintenance of a delicately balanced inflammatory homeostatic environment within. For example, in contrast to control mice, kidneys of germ-free (Gf) mice have been found to have lower IL-4 levels and increased natural killer T cells. After ischemia/reperfusion (I/R) injury to Gf mice, a significant accumulation of CD8 T cells within the kidneys occurs, resulting in more severe renal damage than in control mice. When Gf mice received fecal transplants from control mice, the renal damage from I/R injury was much less than, and comparable with, that in control mice, suggesting a role of gut microbiota in modulating renal inflammation (2).

However, the interaction between the gut microbiome and the kidney and the pathogenesis of renal damage in AKI is complex, and the microbiome effects on renal inflammation may not necessarily exert a general salutary effect. Emal et al. showed contrasting results in that lower expression of the chemokines CX3CR1 and CCR2 in gut flora–depleted mice resulted in attenuated renal damage after I/R injury (3). Additionally, after fecal transplantation from untreated mice, a protective effect on renal damage was lost, suggesting that depletion of gut flora after antibiotic treatment resulted in depletion of the harmful gut microflora while promoting the prevalence of AKI-protective microflora.

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After I/R injury in an AKI mouse model, there is a change in the gut microflora, with a predominance of *Lactobacillus* species, *Clostridium* species, and *Ruminococcus* species and a reduction in *Bifidobacterium* species (4). Regardless of the renal insult, the gut microflora metabolize the D-AAs, but after I/R injury only D-serine was detected in the kidney, and an elevated D-serine/L-serine ratio was found in the urine, feces, and plasma of I/R mice. It was suggested then that the gut microbiota is responsible for D-AA generation, particularly D-serine, inasmuch as no D-AAs, except D-asparagine and D-aspartic acid, were detected in the feces of Gf C57BL/6 (Gf B6) mice before and after I/R. It was also demonstrated that after renal insult, the activity of D-AA oxidase decreases and that of serine racemase increases. D-serine was shown to promote tubular cell proliferation after hypoxic damage and to mitigate hypoxia-induced tubular damage. Interestingly, the renal injury in GfB6 and D-serine–depleted mice was alleviated by the oral administration of D-serine, suggesting a potential therapeutic role of D-serine in AKI (4).

These recent studies suggest that the microbiome plays an important role in the mediation of kidney damage in AKI. However, the interplay appears to be complex, and changes in the microflora may either ameliorate or promote renal damage. It is hoped that over the several coming years, further studies of the microbiome and inflammation, and of the impact of its modulation on the development of renal damage in AKI, will better define these mechanisms and help identify effective therapies to help prevent and treat AKI.

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