

Nephrology Care and Caregivers

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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

By Sonali Gupta, Jose Pichardo, and Joseph Mattana

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.

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

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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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,

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.

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