Primary glomerular disease is an important cause of chronic and end stage renal disease

Chronic kidney disease (CKD) is increasingly recognized as a growing global challenge, affecting up to 16 percent of the adult population (1,2). Although the veritable explosion in type II diabetes is largely responsible for this growth in developed and many developing countries, primary glomerular disease continues to contribute meaningfully to the CKD epidemic (2). These diseases account for roughly 10 percent of CKD cases in the United States and up to 50 percent in other countries (3,4). Primary glomerular diseases contribute to considerable morbidity, cost, and mortality. As part of this, they contribute importantly to ESRD in the United States (Figure 1). More than 80,000 patients with ESRD report glomerulonephritis as their primary cause of ESRD, and 9000 patients with primary glomerular disease begin undergoing dialysis each year (2). In addition to the burden of glomerular disease in adults, it is noteworthy that roughly one in four cases of pediatric ESRD is related to primary glomerular disease (2).

Recent discoveries have focused attention on primary glomerular disease

Whereas many speak of limited progress in the field of glomerulonephritis, and being stuck with treatments similar to those we used decades ago, recent discoveries and trials suggest that advances are indeed being made and are likely to be extended. Minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), and IgA nephropathy (IgAN) cause proteinuria by means of glomerular podocyte injury, most likely related to immune dysregulation, although the exact mechanisms are still unknown (3,4). For populations at risk, the mechanisms of podocyte-related and non-podocyte-related injury, clinical manifestations (including impaired renal function, hematuria, proteinuria, and hypertension), response to corticosteroids and other anti-inflamatory and immunosuppressive therapies, and rates of progression to ESRD differ widely among these diseases. Still, all these conditions have common features that link them together. New insights into their mechanisms are most likely to lead to inroads into prevention and therapy. Genetic mutations that lead to syndromes of podocyte dysfunction and injury have yielded conditions indistinguishable from classic MCD and FSGS (5,6). New findings derived from linkage analyses may elucidate other glomerular diseases such as MN, FSGS, or IgAN (7,8). Defects in specific proteins, such as angiotensin-like 4 protein, may also lead to MCD, and these defective proteins may be specific targets of therapy (9). Specific antibodies have been linked to certain disease states, such as antibodies to galactose-deficient IgA1 in IgAN and antibodies to the M-type phospholipase A2 in MN (10,11). Increased levels of circulating factors such as soluble urokinase-type plasminogen activator receptor have been reported in FSGS and initially appeared to be related to the degree of impaired kidney function (12). These selected examples demonstrate that distinct pathways may be examined in these patients to help define the mechanisms of disease, and these approaches may result in the discovery of biomarkers of the specific disease, prognostic indicators, or novel targets for therapy.

Insights into advances in glomerular disease

Building on these findings, this issue of Kidney News presents some insights and opinions regarding glomerular diseases, ranging from specific discoveries through mechanisms of collaborative studies and proceeding to suggestions about how to further improve the care of patients with glomerular disease, whether primary or secondary to systemic disease. It is hoped that these efforts will usher in more interest, resources, and effort in the area to ultimately benefit the patients we serve.

References


Richard A. Lafayette, MD, FACP, is associate professor of medicine in the Division of Nephrology at Stanford University School of Medicine in Palo Alto, CA. Dr. Lafayette edited this special section for ASN Kidney News.