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Kidney Disease in HIV Infection: Introduction

As early as 1984, physicians in New York and Miami recognized kidney disease as a rare but devastating complication of the acquired immune deficiency syndrome (AIDS). In that same year, scientists at the National Cancer Institute cloned the human immunodeficiency virus (HIV), opening the door to more than 2 decades of active research into the pathogenesis of AIDS and other complications of HIV infection, including kidney disease. The introduction of combination antiretroviral therapy (ART) in 1996 had a dramatic impact on the natural history of HIV, with significant reductions in opportunistic infections and mortality. An unanticipated consequence of prolonged survival has been the increasing prevalence of serious non-AIDS complications, including kidney, liver, and cardiovascular disease, which have emerged as leading contributors to morbidity and mortality in patients with HIV infection.

Early reports of kidney disease in the setting of AIDS described an aggressive form of focal segmental glomerulosclerosis, now known as HIV-associated nephropathy (HIVAN). The majority of affected patients were African Americans or Haitian immigrants, a racial predisposition supported by larger cohort studies and by data from the United States Renal Database System (USRDS). Active investigation during the early and mid-1990s first established a pathogenic link between local HIV infection of the kidney and the development of HIVAN. Epidemiologic data also supported a pathogenic role for HIV, with a plateau in the incidence of HIVAN after the introduction of effective ART. Ongoing investigations continue to identify host responses and host-viral interactions with relevance beyond HIVAN.

Although HIVAN is the classic kidney disease of HIV, even early case series described a spectrum of kidney disease in patients with HIV/AIDS. Although the association with race is less striking for kidney diseases other than HIVAN, the incidence of HIV-related end-stage renal disease (ESRD) is increased markedly among African Americans regardless of the underlying diagnosis. With expanding access to ART and anticipated reductions in AIDS-related deaths in sub-Saharan Africa, HIV-related kidney disease is likely to place a heavy burden on the public health of this resource-limited region. In addition, the overall incidence of HIV-related ESRD does not appear to have declined after the introduction of ART in the United States, despite a decline in the incidence of HIVAN. This may reflect an increase in other HIV-related and comorbid kidney diseases, as well as potential nephrotoxic effects of long-term exposure to HIV infection and ART. The balance of benefit and risk associated with ART is even more complex in sub-Saharan Africa, home to nearly two thirds of the world's HIV-infected population, because of limited resources for kidney disease screening, toxicity monitoring, and ESRD management.

Despite the potential implications of HIV-related kidney disease for global public health, fewer resources are available for the continued surveillance and characterization of kidney disease among patients with HIV infection. The epidemiology of HIV-related kidney disease has been defined using data from large cohort studies and from the USRDS. At the same time that research cohorts face drastic cuts in government funding, the USRDS no longer collects data on HIV infection as a comorbid condition in incident ESRD patients. More than 2,700 people were known to be living with ESRD attributed to AIDS nephropathy at the end of 2005, but this estimate does not include patients with HIV infection and comorbid kidney disease, or patients in states where confidentiality laws limit reporting of HIV-related diagnoses. Future research and public health initiatives will suffer from the loss of these invaluable epidemiologic resources, which have been instrumental in shaping policy and treatment guidelines for patients with HIV infection.

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Against this backdrop, we have invited internationally recognized investigators in HIV-related kidney disease from the fields of nephrology, pathology, and infectious diseases to review topics of direct clinical and public health relevance to an international audience. Lessons learned from the study of HIVAN also provide important insights into the pathogenesis and treatment of other HIV-related kidney diseases, and we have chosen to open this issue with two complementary reviews focused on the classic kidney disease of HIV infection. A concise review of the clinical presentation and epidemiology of HIVAN serves as the framework for Vivette D'Agati's summary of more than 20 years of work to characterize the unique pathologic features of HIVAN. This characteristic pathology also has provided direction for studies of HIVAN pathogenesis in animal models, in vitro experiments, and human kidney tissue, as reviewed by Jeremy Leventhal and Michael Ross.

Although the role of HIV infection in the pathogenesis of non-HIVAN kidney disease has not been established, other glomerular diseases are encountered frequently in patients with HIV. Scott Cohen and Paul Kimmel summarize the literature on immune complex kidney diseases in the setting of HIV infection, including a comprehensive review of available data on pathogenesis and management. In an overview of the differential diagnosis of glomerular disease in patients with HIV, Derek Fine and colleagues discuss thrombotic microangiopathy and other glomerular lesions that should be considered in these patients.

Acute kidney injury is also common among patients with HIV/AIDS. Similar to observations in the general population, acute kidney injury in HIV-infected patients is associated with increased mortality. Studies of acute kidney injury from both the early AIDS epidemic and from the ART era are reviewed in this issue, showing little change in the incidence or etiologies of acute kidney injury with the widespread use of ART. Medication toxicity remains a common cause of acute kidney injury in the ART era, and the potential nephrotoxic effects of available antiretroviral agents are reviewed by Mohamed Atta and colleagues.

Clinical considerations in the management of kidney disease in HIV-infected patients have been reviewed in guidelines published by the Infectious Diseases Society of America. Several important topics in clinical management are updated in this issue, with a focus on areas in which new data are available. Jonathan Winston reviews the clinical assessment of kidney function in patients with HIV, including recent data on the utility of cystatin C in this population. The management of ESRD in patients with HIV infection, in particular the safety and feasibility of kidney transplantation, is reviewed by Deirdre Sawinski and Barbara Murphy. Unique considerations in the diagnosis and management of HIV-related kidney disease in children are discussed by Mignon McCulloch and Patricio Ray, with a particular focus on the large pediatric population in developing countries.

Particularly in resource-limited settings, patients with HIV infection and AIDS are at increased risk for co-infections that may be associated independently with kidney disease. Although the hepatitis viruses are the most commonly implicated co-infections, a variety of other infectious agents also have been associated with specific kidney diseases. In the final article in this issue, Jeffrey Kopp discusses other viral-mediated kidney diseases that can occur in patients with and without HIV infection.

With the aging of the HIV-infected population in the United States and western Europe, and expanding access to ART in the developing world, nephrologists and HIV providers will be asked to manage an increasing number of patients with HIV and kidney disease. We would like to thank our friends and colleagues who have contributed their time and expertise to make this issue an important resource for providers involved in the care of this growing patient population.

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