Warning: Kidney Virus Detected

> The variety of genes on the planet in viruses exceeds, or is likely to exceed, that in all of the rest of life combined.
>
> —Edward O. Wilson

In 1993, the number of viruses that infected vertebrates, specifically mammals, was estimated at 1,000,000 and 320,000, respectively.[1] By 2012, 219 human virus species had been identified, with 3–4 novel viruses projected to emerge each year from mammalian and avian reservoirs.[2] Advances in genetics during the past few decades have facilitated the detection of more and more occult viruses, previously unrecognized within the human genome, the accumulation of which is collectively known as the human virome. Many of these viruses are probably commensals, freeloaders taking a reproductive ride on human DNA, but 23 families of pathogenic viruses have also been identified.[3] In this issue of *Advances in Chronic Kidney Disease*, our panel of experts discusses clinical disorders caused by viral infection of native kidneys.

Sir Peter Medawar once opined, "a virus is a piece of bad news wrapped up in protein," so naturally, the bad news for the kidneys begins with fusion of the viral envelope with the host cell membrane.[3,4] Dr. Bruggeman discusses the cell biology common to viruses that infect human kidneys. Specifically, disease development requires viral tropism for the kidney; subversion of the cellular machinery, causing either cell lysis or latent infection; and host responses to this attack. Ironically, this last event, the counterattack by the innate and adaptive immune system, may be one of the most important factors in damaging the renal parenchyma, even if the virus itself is eradicated.[5] Also considered in this review are novel infections that may contribute to immunoglobulin A nephropathy, focal and segmental glomerulosclerosis, and nonspecific features of chronic kidney disease.

Our tour begins with the hepatitis viruses, which contribute significantly to global epidemic and endemic infections. By definition, hepatitis A and B viruses (HAV and HBV, respectively) primarily infect the liver, but the impact of these viruses on the kidneys may be substantial. Drs. Andrievskaya, Lenhart, and Uduman consider the epidemiology of HAV, including recent spikes in incidence in many regions of the United States. When HAV causes fulminant hepatic failure, critical illness with acute kidney injury is a frequent and ominous development.[6] In this case, an ounce of prevention with HAV vaccination is more than worth a pound of cure with liver transplantation. HBV is the most common chronic viral infection in the world, affecting >400 million people, and HBV-mediated immune complex disease may present as membranous nephropathy and polyarteritis nodosa.[7] Drs. Soman and Soi discuss systems-based interventions to decrease transmission of the highly contagious HBV among patients requiring hemodialysis.

Acquired immune deficiency syndrome, caused by human immunodeficiency virus (HIV), has matured from a terminal diagnosis in the 1980s to a chronic disease today. Similarly, HIV-associated nephropathy, once a common cause of collapsing focal and segmental glomerulosclerosis and end-stage renal disease in HIV-infected African-American patients, has nearly vanished from populations with access to combination antiretroviral therapy.[8] Kidney disease in patients infected with HIV is now caused by different pathophysiological processes, such as immune complex deposition and thrombotic microangiopathy, as well as by toxicity from antiretroviral medications themselves. Drs. Perazella and Sury review the changing face of HIV-associated kidney disease and its multifarious etiologies, with particular attention to a novel, less noxious formulation of the antiretroviral drug tenofovir.

Finally, the viral hemorrhagic fevers (VHFs), caused by an assortment of exotic, zoonotic viruses, are also associated with significant kidney disease. Patients with these infections may be critically ill, with hemorrhagic and hypovolemic shock and consequent multiorgan failure.[9] A subset of these patients, approximately 100,000 cases annually, presents with hemorrhagic fever with renal syndrome, which is characterized by increased vascular permeability, coagulopathy, glomerular disease, and acute kidney injury.[10] Flaviviruses make up a disproportionate share of etiologic agents for VHFs, including dengue, yellow fever, West Nile, and Zika; Hantavirus and Ebola round out this lethal list.[9] Drs. Burdmann, Prasad, and Patel review the epidemiology, pathophysiology, and clinical presentation of VHFs. Drs. Prasad, Novak, and Patel also consider parvovirus, which may present with arthropathy, myelosuppression, and glomerular disease.

In conclusion, although a vast variety of viruses infects humans and many cause kidney disease, the articles that follow represent a survey of only the most common pathogens. Indeed, Marc Lipsitch sagely prophesied, "we can't predict what a virus we've never seen will do," and it seems likely that nephrotoxic viruses will continue to emerge to plague humanity.[11] Meanwhile, the current issue of *Advances in Chronic Kidney Disease* should be educational and entertaining for nephrologists, virologists, and others curious about the malware that infects the kidneys.

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