West Nile Virus: Don’t Underestimate Its Persistence

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An interesting report in this issue of the Journal by Murray et al [1] provides compelling evidence that West Nile virus (WNV) can persist for years in the kidneys of humans convalescing from infection with this virus. Furthermore, WNV, as detected in the form of genomic RNA, was excreted in the urine for 6 years or more after recovery from acute disease. As discussed below, these findings could have important implications for flavivirus epidemiology and pathogenesis.

One of the many questions that occupy the minds of virologists is, what do pathogenic viruses do when they are not causing overt disease transmission? We are all familiar with the concept of acute viremic infections from which the infected host either recovers or dies, and the general feeling has been that after recovery the virus is cleared from the host. However, we also recognize chronic infections during which the virus appears to persist in the host, often causing long-term sequelae; hepatitis C virus springs to mind. Alternatively, some veterinary RNA viruses are known to cause asymptomatic persistent infections in their apparently healthy hosts, spasmodically emerging for one reason or another to cause fresh outbreaks in susceptible hosts. Most virologists would probably classify WNV as being in the acute infection category, although there is some evidence that this virus may be able to persist in its infected host beyond the period of recovery, as indeed appears to be the case with some related arthropod-borne viruses, such as yellow fever virus and Japanese encephalitis virus.

The report by Murray and colleagues is important for many reasons but particularly because it begins to provide robust evidence for WNV persistence in humans. First, the authors demonstrate that several of the studied convalescent patients were WNV positive in first-round reverse-transcription polymerase chain reactions >6 years after the acute infection period. Second, whole genome sequences were obtained from 80% of the positive samples. These 2 observations strongly imply that the virus was replicating during the period of chronic/persistent infection. Third, one of the WNV-positive patients, who originally had encephalitic infection, recovered completely and did not present with any further clinical symptoms, implying that even apparently healthy (ie, fully recovered) individuals may be carriers of the virus. Fourth, viral RNA was detected in the urine for at least 6 years after infection, implying long-term replication of the virus in the kidneys, analogous to laboratory models of WNV persistence in hamsters. Fifth, one of the patients developed kidney failure after his illness. These findings therefore also have important implications for public health in the face of infection with WNV and related flaviviruses.

Finally, one can ask, what is the significance of these findings to WNV transmission? Nonviremic transmission of WNV between mosquitoes cofeeding on mice [2] and nonviremic transmission of Japanese encephalitis virus [3] from healthy nonviremic bats to feeding mosquitoes have both been reported. The findings of Murray and colleagues could therefore also raise important issues concerning the potential for WNV and other related flaviviruses to be transmitted to mosquitoes by apparently healthy humans or animals (assuming a similar pattern of WNV behavior in animals) and thus potentially initiate epidemics in new regions of the world. Could this be the method by which WNV arrived in North America in 1999?

References