West Nile virus (WNV) is a member of the flavivirus family, which includes agents that cause such important diseases as yellow fever, Japanese encephalitis, dengue fever, St. Louis encephalitis, and Central European encephalitis. The flaviviruses are one of the most important of the arthropod-borne viruses (arboviruses), with the mosquito being the arthropod vector for a number of these viruses, including WNV.

The flaviviruses occupy a special place in the history of both human disease and the advancement of our understanding of viral infection. For example, the yellow fever virus was the first “filterable” agent shown to cause human disease. Further, flaviviruses were among the early examples of how international travel can lead to the spread of disease, with yellow fever believed to have been introduced into the Americas by mosquito-infested slave ships transporting people from West Africa. Epidemics of yellow fever within the United States have been well documented. Indeed, WNV is the latest of a number of flaviviruses to be imported into North America.

Most people within the United States were probably ignorant of the existence of WNV prior to 1999. Successive seasons that have seen the migration of the infection north, west, and south of the 1999 epicenter in New York, however, have contributed to increased public health concerns, expanded efforts in public education, and substantial media attention.

Where did WNV come from? In part, this may be answered by the name of the virus. The first reported isolation of the virus occurred in the West Nile district of Uganda in 1937 and was reported by Smithburn and associates in the American Journal of Tropical Medicine in 1940. Yet, the virus is not limited to Africa. The virus has been reported in most of Africa, the Middle East, Russia, parts of Europe and Eurasia, the India subcontinent, and parts of Southeast Asia. Prior to the appearance of the disease in North America, severe outbreaks of disease were reported in Russia (1999) and in Romania (1996).

Based on current evidence, the U. S. outbreak appears to be the result of the carriage of WNV from the Middle East via viremics migratory birds, although there have been suggestions that the illegal importation of infected birds may have been a factor. There is growing evidence to support migratory birds as a carrier of WNV. Indeed, birds represent the major reservoir of the virus; and when introduced into a naive environment, the virus can have a devastating impact on native species not previously exposed. Thus, in North America, species such as the American Crow were severely impacted after the emergence of the disease in 1999, as were many exotic birds housed within the Bronx and Queens zoological gardens.

In addition to the evidence supporting migratory birds as the introductory hosts, there is evidence that mosquitoes that feed on birds (ornithophilic mosquitoes) probably introduce the virus into a domestic host bird species, allowing virus amplification. From birds, other species — including humans and horses — may be infected, although these are not considered to be primary hosts.

The occurrence of the virus in native bird species and associated deaths led to surveillance schemes whereby bird species have been monitored, particularly in winter and fall, for concentrations of abnormal die-offs. Dead birds may be tested for WNV and, if found to be infected, health authorities can implement appropriate surveillance and mosquito-control measures.

As the epidemic spread and intensified from 1999 to 2002, the Centers for Disease Control and Prevention (CDC) and health laboratories became inundated with specimens, taxing their capacity to meet demand. As a consequence, the Food and Drug Administration (FDA) called upon industry to develop commercially available assays to support clinical laboratories across the United States. For the 2003 season, two companies had WNV diagnostics cleared by the FDA: PANBIO’s IgM capture ELISA and assays developed by Focus Technologies. For the 2004 season, PANBIO has the next-generation assay currently submitted to the FDA for evaluation.

The cooperation of the CDC, FDA and state health authorities, together with the assistance of a number of private reference laboratories, was pivotal to the capacity of our team.
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Without the determination of government authorities to address this emerging health threat, progress would have been slow.

West Nile Virus

Welcome home, troops!

Major Martin E. Tenney, MEDCOM-HQ, featured in MLO’s December 2003 tribute to military medical laboratory technicians returned safely home in March from his tour of duty in Iraq.

Stuart Hazell, PhD, is vice president, Research and Development at PANBIO. He was in charge of the WNV assay development within the company, supported by a team of professional laboratory scientists. He is an honorary professor of microbiology at the University of Southern Queensland in Australia.

To build an assay, validate for the FDA, and then release a kit to market within a six-month time frame. Without the determination of government authorities to address this emerging health threat, progress would have been slow.

The volume of testing conducted across the United States in 2003 highlighted the need for commercial assays. It has been estimated that on the order of 500,000 to 1 million samples were tested in 2003. Increased testing may have revealed more cases earlier. The CDC reported 9,175 cases of WNV infection and 230 deaths in 2003. While the number of reported cases was up from 4,156 in 2002, the number of deaths was down from 284 in 2002. This latter statistic may relate to greater awareness by the public and health authorities — leading to earlier diagnosis and treatment of disease, rather than a decline in the virulence of the circulating strain.

What of 2004? It would be unwise for anyone to make any claim as to how the 2004 season (starting June) may unfold. WNV may continue on a westward path, leading to increased cases along the western seaboard of the United States. There may be resurgence of infection along the Atlantic coast and/or in the Mississippi states. The infection may become endemic with a lower incidence across the country. Based on an assessment of the 1999-2003 pattern of infection, any or none of the above may occur.

In 2004, there will be a greater reliance on commercial diagnostic tests. The CDC is no longer supplying state health laboratories with antigen for “in-house” assays, and stocks held within the public health laboratories were depleted in 2003. There will also be greater demand for hospital and local laboratories to undertake testing to improve the turnaround in test results. While we may wish for WNV to return to whence it came, this appears a forlorn hope at present.