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West Nile Virus and Its Appearance in the U.S.

The West Nile Virus (WNV) was first described in Africa in 1937. In a serosurvey of African trypanosomiasis in the West Nile District of Uganda, Kenneth C. Smithburn at the Rockefeller Institute encountered a febrile woman who otherwise felt well. Her blood was subsequently injected into 10 Swiss albino mice, nine of whom died. Then, blood from the sick mice was injected into healthy mice. These healthy mice also died. A virus was isolated and was subsequently shown to be a flavivirus. The Latin prefix "flavi" means yellow since the Yellow Fever virus was one of its most notorious members. In 1943 it was confirmed that mosquitoes were the vector for both birds and mammals for West Nile Virus.

In the 1950s, R.M. Taylor studied transmission patterns between ticks, birds, mice, and other arthropods and noted the ability of the virus to lay dormant within pools of insects and animals for years. Surprisingly, they found anti-WNV positive results in serologic samples from 1.4% in the Congo to 46.4% in Sudan. Serosurveys in the 1940s and 1950s in Egypt showed over 90% of individuals over 40 years of age had anti-WNV antibodies. In Egypt, the virus was subsequently isolated from patients, birds, and mosquitoes.

Not until 1957 was West Nile Virus recognized as a major illness. An epidemic occurred in Israel with over 500 infected patients diagnosed with West Nile Virus infection over several months. Unlike previous cases in which symptoms were self-limiting, meningoencephalitis with mental status changes and neurologic manifestations was the primary clinical presentation. The mortality was 8.2% in elderly patients in nursing homes. Romania's outbreak in 1996 led to an unprecedented number of CNS infections, with 762 out of 835 patients contracting encephalitis with 17 deaths.

The New York City Outbreak

By early 2000, West Nile Virus outbreaks seemed to increase in frequency across Europe and North America. A dramatic appearance of West Nile Virus occurred in 1999 in New York City. In the summer of 1999, physicians at Flushing Queens Hospital admitted an unprecedented number of patients with encephalitis and meningitis. These cases were reported to the Centers for Disease Control and Prevention in Atlanta (CDC). The CDC initially diagnosed the encephalitis-causing virus as the St. Louis Encephalitis (SLE) virus based on a weak antibody reaction to SLE virus.

From August to September 1999, 48 cases of meningoencephalitis of uncertain etiology were found in New York City. The brain samples from five patients were sent to Dr. Ian Lipkin, director of the Emerging Infections Laboratory of the University of California, Irvine. Lipkin had isolated a flavivirus from these samples and then sequenced the genome of the virus. Within 24 hours, they found the genome to be related to West Nile Virus.

Weeks prior to the human outbreak of West Nile Virus, 87 birds of various species were found dead in Central Park, NY. This anomaly was initially attributed to chemical

poisoning until zookeepers at the Bronx Zoo and Queens Zoo discovered dead birds in their cages. The autopsy reports from these birds failed to reveal the cause of death; no known toxins, bacteria, or viruses were isolated. Similar to the New York patients, meningoencephalitis and myocarditis were found in autopsies of the birds as the cause of death.

In late August 1999, Dr. Beverly Schmitt at the U.S. Department of Agriculture National Veterinary Service Laboratory in Ames, Iowa found evidence of a virus in cell culture inoculated with tissue of birds that had died. The visualization of the virus by electron microscopy showed that it resembled flaviviruses or togaviruses. The CDC laboratory in Fort Collins identified the virus as West Nile Virus using stored anti-sera.

The Role of the Mosquito

Once in North America, the West Nile Virus infected native species of mosquitoes. Different types of mosquitoes were found to be responsible for the transmission of disease in humans. "Amplification" mosquitoes include *Culex pipiens* and *Culex restuans*. These mosquitoes feed on birds and transmit the virus to other birds creating a large reservoir of West Nile Virus infection. The "bridging" species include *Coquillettidia perturbans*, and human biters include *Aedes vexans*. The latter 2 mosquitos feed on both birds and humans and transmit the virus. The Asian Tiger mosquito (*Aedes albopictus*), a species native to Asia is a known vector for West Nile Virus. It was isolated in Baltimore, MD in 1999 and subsequently linked to West Nile Virus infections in birds and humans in the U.S.

Current Status

In 2000, one year after the New York City outbreak, 20 more patients were diagnosed with West Nile Virus infection in New York state and neighboring states. West Nile Virus infection has now been reported across the United States. West Nile Virus has a broad ecological network of infection among birds, mammals and insects. Increasingly rainy springs paired with warmer summers allow mosquito populations to flourish. Bird migration patterns in spring and fall were thought to account for the spread of the virus throughout the U.S. Unlike the populations in Uganda and Egypt, North American populations were more vulnerable and the virus appeared more virulent. Before arriving in North America, transmission from person-to-person had never been documented. However, in the U.S., West Nile Virus transmission occurred via blood transfusion, organ transplant, intrauterine exposure, and breast feeding. By 2008, more than 28,000 Americans were infected by the virus. Over 11,000 contracted encephalitis and over 1,000 died. The emergence of West Nile Virus in North America correlated directly with the precipitating decline of the bird population. Since the 1999 New York City outbreak, 45% of the U.S. crow population has died. In 2012, Arthur Leis, a neurologist in Jackson MI, who reported the first case of poliomyelitis syndrome in West Nile patients suggested that the virus had become more virulent based on the number of encephalitis complications observed in his patients.

References

1. Beran, G. W. & Steele, J. H. (Eds.). (1994). Handbook of zoonoses: Section B: Viral (2nd ed.). Boca Raton, FL: CRC Press.

2. Despommier D. West Nile Story. Apple Trees Productions, LLC, 2001. New York, NY.

3. Nash, D. et al. (2001). The outbreak of West Nile virus infection in the New York City area in 1999. New England Journal of Medicine, 344 (24), 1807 – 1814.

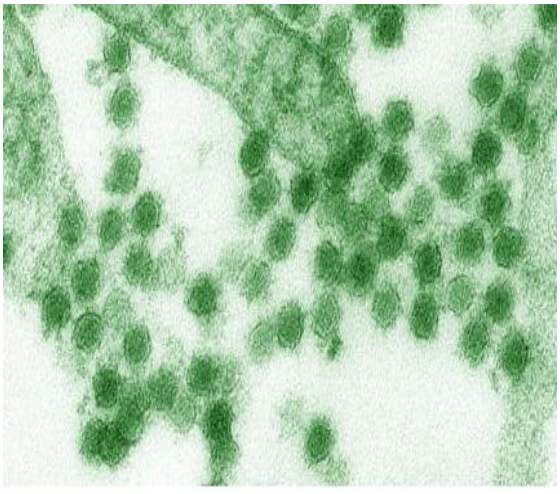
4. Newman W, Southam CM. Virus treatment in advanced cancer. A pathologic study of 57 cases. Cancer 1954;7:106-118.

5. Oldstone, M. B. A. (2010). Viruses, plagues, and history: past, present, and future. New York City: Oxford University Press.

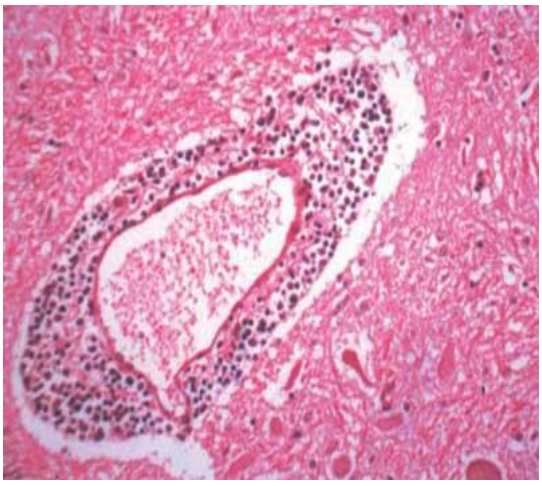
6. Smithburn KC, Hughes TP, Burke AW, Paul JH. A neutropic virus isolated from the blood of a native of Uganda. Am J Trop Med. 1940;20:471-492.

7. Vastag B. Hints of a more virulent, mutating West Nile Virus emerge. Washington Post, Nov. 8, 2012.

Figures



University of Wisconsin-Madison – Department of Bacteriology: West Nile Virus.
Electron micrograph.



West Nile Virus Lymphocytic Perivascular Infiltration
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