

HEALTH EFFECTS

REVIEW

Arboviruses - West Nile Virus**Introduction**

Arboviruses (arthropod borne viruses) are a group of viruses that infect humans and spread disease via the bite of blood sucking arthropod vectors, such as mosquitoes and ticks. There are many viruses in this group, some causing diseases like the well-known dengue and yellow fever, while others cause more exotic-sounding diseases such as o'nyong-nyong fever. This is a diverse group of viruses whose common feature is transmission by the bite of a mosquito.

Arboviruses are not just curiosities of tropical climes or long forgotten epidemic scourges in temperate climates, however. Yellow fever was once epidemic in northern North America and could make resurgence under the right circumstances. And other arboviruses, such as those that cause encephalitis (brain inflammation), are currently endemic in North America, with periodic epidemic outbreaks.

Up until the appearance of the West Nile Virus (WNV) in New York in 1999, the four most common mosquito-borne brain inflammations in the United States and Canada were the California encephalitis serogroup (CAL), St. Louis equine encephalitis (SLE), western equine encephalitis (WEE), and eastern equine encephalitis (EEE). The majority of the CAL encephalitis cases are caused by one of its members, the La Crosse virus. West Nile virus and St. Louis encephalitis are members of the Flaviviridae family, eastern and western equine encephalitis viruses of the Togaviridae family (genus Alphavirus), and LaCrosse virus of the Bunyaviridae family. In the temperate zones, cases occur primarily in the late summer or early fall, following the mosquito season.

The majority of infected humans show no symptoms or only mild flu-like symptoms. Arboviruses can cause fever, headache, body aches, skin rash and swollen lymph glands. Severe infection may result in coma, tremors, convulsion, paralysis, encephalitis, and occasionally permanent neuro-logic sequelae or death. Encephalitis is an acute inflammatory process that affects brain tissue. The meninges, the membranes that cover the brain are also inflamed, giving rise to another type of brain inflammation: meningo-encephalitis. The U.S. Centers for Disease Control and Prevention (CDC) defines a confirmed case as febrile illness with mild neurologic symptoms, aseptic meningitis, or encephalitis with either fourfold or greater rise in serum antibody titer, viral isolation, or specific immuno-globulin M (IgM) antibody in cerebrospinal fluid[1] Antibiotics are ineffective against viruses and no vaccines are currently commercially available for arboviral diseases. Treatment is limited to relieving the symptoms of the infection and dealing with complications such as brain swelling and difficulty breathing[2]. The only way to prevent infection are personal protective measures like insect repellent and protective clothing, and public health measures that reduce the population of infected mosquitoes. Measures include eliminating insect breeding areas, killing of larvae and adult mosquito's. Unfortunately, this type of mosquito control is not always effective in interrupting the transmission of human disease during outbreaks.

West Nile Virus

Up until 1999, when it was identified in New York, the West Nile virus had not been reported in North America. Commonly found in Africa, West Asia, and the Middle East, WNV spread from New York and infected birds has since been reported in over 14 states(2). In 1999, 62 cases of severe disease occurred in New

York. Seven people died, including a 75-year old Canadian who had visited New York City in September 1999, who passed away after returning to Toronto(3). In 2000, 17 cases were reported including one death(4). As 2004 comes to an end, 14 Canadian deaths have been confirmed (5). This is in stark contrast to 2001 where there were no human cases detected in Canada, but WNV had been detected in 122 birds throughout Ontario (6).

The West Nile Virus was first isolated in Uganda in 1937 from the blood of a febrile woman and epidemics have occurred in Israel (1951-4, 1957), France (1962), South Africa (1974), Romania (1996), and Russia (1999). Temperate climates in Romania and Russia are similar to the ones found in Canada and the US (2).

The mode of transmission for WNV is primarily by the mosquitoes *Culex pipien* (the common house mosquito) and *Aedes* spp., which feed on birds and mammals. However many species are capable of carrying the infection, and we can expect other mosquito species to become important in specific localities. The appearance of WNV in Florida suggests transmission of this virus by *Cx. nigripalpus*, a primary vector of SLE virus in that state. While some birds, like the American black crow and the Blue Jay, are seriously affected by the virus, others like the common house sparrow develop unapparent infections that can still spread the disease. Birds serve as a reservoir for the virus but humans, horses, and other mammals are thought to be dead-end hosts, and as such, are not important for its spread. West Nile virus has also been found in cats, chipmunks, skunks, bats, squirrels, rabbits, and raccoons (7,8). There is still much to be learned about this virus, however, and our views of the role of non-avian species in disease spread might change.

There is no evidence at this point that humans can get the virus from birds, or that a human can infect another human. However, vertical transmission (adult egg adult) has been shown. It is probable, however, that the disease survives the winter in hibernating adult mosquitoes that re-emerge in the spring, bite a bird and continue the cycle. According to the CDC, the chances that a person bitten by an infected mosquito will become severely ill is less than 1%, and even during an outbreak, most mosquitoes are not infected (9). Among those with severe illness, case fatality rates range from 3% to 15%. The disease is rare in children and most severe in people with weakened immune systems and the elderly.

A study in Egypt reported that 50% of the people exposed to the virus developed antibodies but showed no symptoms. Symptoms appear 3 to 15 days after infection and include fever, headache, sore throat, backache, and fatigue. Severe cases may result in acute aseptic meningitis or encephalitis.

Other Arboviruses

The LaCrosse virus was first identified in LaCrosse, Wisconsin in 1963. Common in the upper Midwestern United States, La Crosse virus is transmitted by the day-time biting tree-hole mosquito, *Aedes triseriatus*, and its principal vertebrate hosts are eastern chipmunks, gray squirrels, and red foxes. While 90% of the symptomatic cases occur in children under 16 years of age, La Crosse encephalitis is rarely fatal, with death occurring in less than 1% of cases [9]. LAC is often misreported as aseptic meningitis or viral encephalitis of unknown etiology because physicians do not request tests necessary for identifying the LAC virus.

St. Louis encephalitis cases (SLE) are widespread throughout the US with as many as 2000 cases reported during large outbreaks. The last nationwide epidemic in the US occurred in 1975 and resulted in 1815 human cases in 31 states [10]. This virus is the most common cause of arboviral meningitis outbreaks in Canada [11]. A short-lived epidemic in southern Ontario (bordering the U.S.) occurred in 1975, resulting in 66 cases. *Culex pipiens quinquefasciatus* is the mosquito responsible for the majority of virus transmission to humans. Children and the elderly are the most susceptible, with a 20% mortality rate in the elderly [12]. SLE is a natural infection found in wild birds. Similar to WNV, house sparrows are thought to be a principal reservoir for the virus. The WNV outbreak in New York was originally believed to be SLE.

Western equine encephalitis (WEE) is found primarily in the western US and south-central Canada. Human cases in Canada have occurred most often in Saskatchewan and Manitoba [13]. Disease occurs most often in infants and young children. Cases are usually asymptomatic or mild, with a mortality rate of about 3%. Of the severely affected infants, 90% have seizures and 50% of infants with seizures have permanent neurologic deficits. WEE has been isolated in a variety of mosquito species including *Culex tarsalis*, *Aedes dorsalis*, and *Aedes melanimon*. No human cases of WEE have been reported since 1994, and only three were reported since 1990, suggesting that WEE is poorly recognized and under diagnosed [14].

First identified in the 1930s, eastern equine encephalitis is the most severe of the arboviral encephalitides seen in the US and is most often found along the Atlantic and Gulf coast regions. Incubation time ranges from four to ten days and early symptoms include fever, muscle pains, and headaches. Although fewer than ten human cases of EEE are reported annually in the US, it is an extremely serious disease with mortality rates during epidemics reaching 70% [15]. Of those that do recover, many will suffer permanent brain damage. There have been no recognized human cases in Canada, but the virus has been detected in horses in Quebec and Ontario [16].

The natural cycle of EEE includes birds and the mosquito *Culiseta melanura*. This mosquito is not a human biter. The virus leaves the natural cycle via bridge vectors such as *Coquilletidia perturbans* and *Aedes sollicitans*, which feed on birds and humans.

Status of Arboviral Infection

Over the past decade, the number of arboviral encephalitis cases reported to the CDC has fluctuated between a low of 45 in 1992 to a high of 132 in 1996. This year-to-year fluctuation is characteristic of these diseases. At the moment we do not understand why one year is bad and another has no or few cases. Because arboviral diseases are part of a complex ecological interaction between the environment where mosquitoes breed, and where birds and humans live, predictions are difficult to make, leaving us to generalize. One generalization is especially that any attempt to eliminate these diseases by eliminating mosquitoes after they become adults, is bound to fail. Mosquitoes breed quickly and in large numbers, making them a powerful force of nature.

Conclusion

With the emergence of West Nile Virus in North America, arboviral encephalitides are once again a major topic of public health attention, although they have been a constant feature of the public health landscape for a long time. Surveillance is crucial for determining the severity of these arboviruses. Often, due to their non-specific flu-like symptoms, cases go undiagnosed. Proper education on avoiding arthropod bites, effective environmental control to prevent excessive breeding opportunities for mosquitoes, and prudent avoidance of panic-induced measures such as broadcast spraying against adult mosquitoes are the indicated responses at the present moment.

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Review Coordinator: Verónica Maria Vieira, M.S.
Senior Science Advisor: Dr. David M. Ozonoff

For further information please contact Jim Houston, Secretary, Health Professionals Task Force
E-mail: houstonj@ottawa.ijc.org

