The West Nile Virus and the dialysis/transplant patient

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Understanding Viruses

Viruses are microscopic particles that contain genetic information surrounded by a protein shell that protects the virus as it travels from cell to cell or from organism to organism. The protein shell also helps the virus develop its genetic information into the susceptible cell. A virus can only survive by living inside of the cells of another host organism. For this reason, some scientists do not consider viruses living things, since they cannot survive on their own.

In the case of the West Nile Virus, individual virus particles are introduced into the bloodstream of a host through the bite of an infected mosquito. The virus then travels through the bloodstream to find a suitable cell in the body in which it can replicate. Successful replication creates many new virions that then return to the bloodstream and look for additional cells to enter and use to replicate (Sfakianos, 2005).

Origins of WNV

In 1901, scientists discovered mosquitoes and ticks could transmit encephalitis. This finding advanced the understanding of how viral encephalitis originated. Collectively, these newly discovered viruses became known as arthropod-borne viruses, or arboviruses. These encephalitic arboviruses were further classified into four groups––A, B, C, and D––based on the symptoms of the disease and the region in which they were discovered. The group B arboviruses were eventually placed into the family, Flaviviridae, which was named after the disease yellow fever, which is caused by one species in the family (the Latin term flavus means yellow). Today, there are more than 70 identified viruses in the Flaviviride family, one of which is West Nile Virus (Sfakianos, 2005).

WNV emerged in recent years in temperate regions of Europe and North America, presenting a threat to public and animal health. The most serious manifestation of WNV infection is fatal encephalitis in humans and horses, as well as mortality in certain domestic and wild birds. WNV was also a significant cause of human illness in the United States in 2002, 2003, and 2004, according to the Centers for Disease Control and Prevention.

WNV was first isolated from a febrile adult woman in the West Nile District of Uganda in 1937. The ecology was characterized in Egypt in the 1950s. The virus was recognized as a cause of severe human meningitis and encephalitis in elderly patients during an outbreak in Israel in 1957. Equine disease was first noted in Egypt and France in the early 1960s.

WNV first appeared in North America in 1999, with encephalitis reported in humans and horses. The identification of WNV in tissue samples from the cases in the United States was surprising and alarming. In a matter of weeks, a single report of two cases of encephalitis in New York led to the identification of a virus that has never been seen before in the Western Hemisphere. The summer of 1999 marked the first time that the WNV was detected in the United States. In this single outbreak, 62 human encephalitis cases were reported; the disease resulted in the death of 7 of these people. The subsequent spread in the United States is an important milestone in the evolving history of this virus (see Table 1 for timeline).

Thirty-seven states have reported 1,299 cases of human WNV in 2005 (see Table 2 for breakdown). This is lower than the 1,386 cases reported in 2004, according to the CDC. Among the cases reported in 2004, 29 deaths occurred. Among the 2005 cases, 230 were linked to blood donation.

There were concerns among health officials about the potential threat of spreading WNV after Hurricane Katrina. The Louisiana Department of Health and Hospitals reported 19 new West Nile cases around the state and said there could be additional cases due to the massive flooding in the New Orleans metropolitan area. Many evacuees were

TABLE 1. TIMELINE OF MAJOR FLAVIVIRIDAE OUTBREAKS

1901	Yellow fever virus transmission by mosquitoes discovered
1917	Australian X outbreak
1927	Yellow fever virus isolated
1932	Yellow fever virus vaccine developed and used in humans. St. Louis encephalitis virus outbreak in Illinois.
1933	St. Louis encephalitis virus outbreak in Missouri
1934	Tick-borne encephalitis virus outbreak in the Soviet Union
1945	Tick-borne encephalitis virus outbreak in central Europe
1951	Australian X outbreak. West Nile virus outbreak in Israel
1953	WNV outbreak in France and Israel
1957	WNV outbreak in Israel
1966	WNV outbreak in Romania
1974	WNV outbreak in South Africa
1996	WNV outbreak in Romania
1998	WNV outbreak in Italy and Israel
1999	WNV outbreak in northeastern United States
2000	WNV outbreak in United States
2001	WNV outbreak in Canada
2002	WNV outbreak in the Caribbean

covered with mosquito bites when treated at triage centers. The hurricane may have disrupted mosquito breeding grounds, state epidemiologist Raoult Ratard said in a statement. "Mosquitoes will become very abundant in flood waters and after a period of drying, we expect to start seeing more mosquitoes and people will be at a greater risk of being infected."

The CDC provides information on mosquito types in the Louisiana area at www.cdc.gov/ncidod/dvbid/westnile/wnv_hurricane.htm and general information on WNV at www.cdc.gov/ncidod/dvbid/westnile/prevention_info.htm.

The impact on dialysis and transplant patients

Along with Hepatitis B, C, and HIV, the WNV adds a new concern to the dialysis and transplant personnel on how to deal with this new pathogen. The most recent case of WNV was reported this past month in New York (see Transplant Update, *NN&I*, p. 36). Below is a review of other cases reported by the Centers for Disease Control and Prevention that have a direct relation to the WNV and the dialysis and kidney transplant population.

2002

In 2002 a recipient of a cadaveric kidney developed a febrile illness 13 days after transplant, which progressed to encephalitis requiring transient mechanical ventilation. Cerebrospinal fluid was positive for WNV IgM antibody. A second kidney recipient had a febrile illness 17 days after transplant, progressing to fatal encephalitis. Brain tissues obtained at autopsy were strongly positive for WNV (Monthly Morbidity and Mortality Report, Sept. 6, 2002). WNV infection in organ transplant recipients had not been reported previously, and the risk for transmission of WNV through donated organs is not known. Of 33 cases reported from 17 states, WNV occurred among persons who had confirmed or probable WNV infection and had received blood components in the month before illness onset. Evidence that WNV can be transmitted through blood transfusion has been found in six of the 33 cases (MMWR, Nov. 1, 2002).

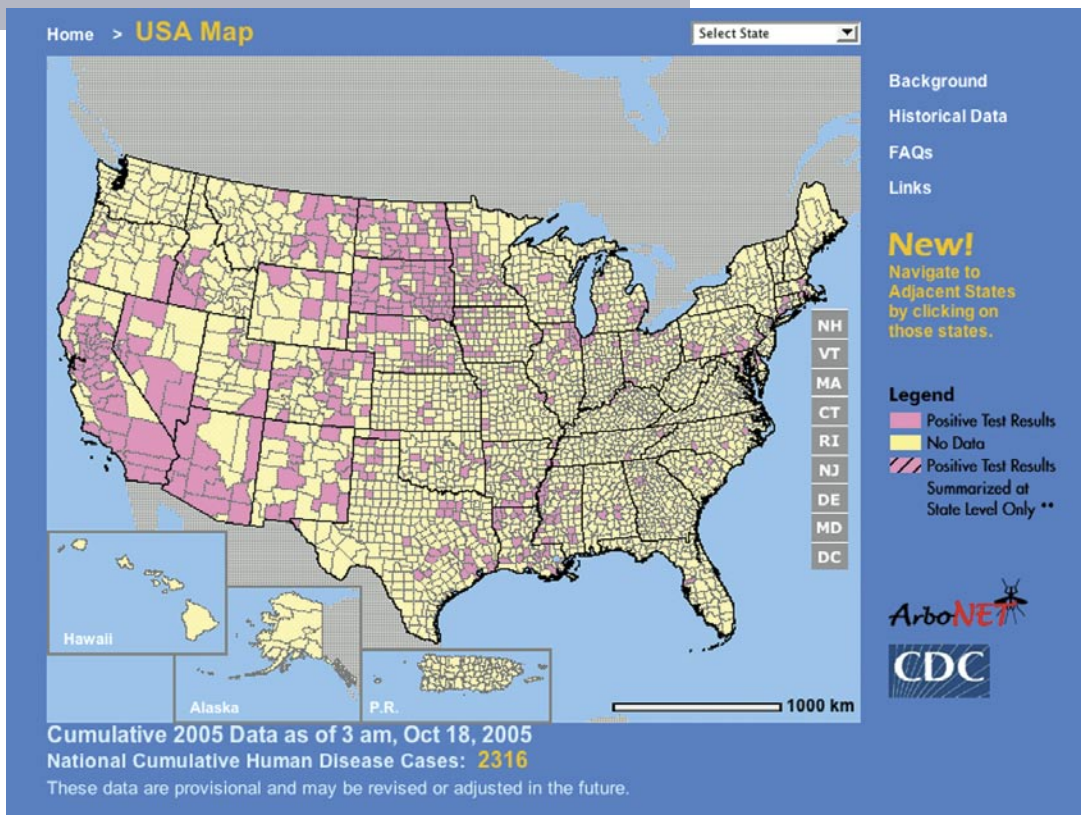
2003

In October 2003, the Georgia Division of Public Health was notified of two patients from the same county with confirmed WNV who had received hemodialysis on the same day and on the same dialysis machine. The two dialysis patients had the only confirmed cases of human WNV disease reported in their county in 2003. Review of the dialysis center's records indicated that another patient had received dialysis on the same machine between these two patients on the same day. The epidemiologic investigation suggested that WNV might have been transmitted at the dialysis center (MMWR, 2003).

In the United States, transmission of bloodborne pathogens such as hepatitis B and hepatitis C viruses has occurred in health care settings. The majority of the outbreaks of hepatitis viruses among hemodialysis patients were caused by cross-contamination of supplies, equipment, or medication, and lapses in infection control practices. Dialysis patients are highly susceptible to infections because they often are immunocompromised and are routinely exposed to invasive techniques and devices (CDC recommendations, 2001). The possibility that WNV might be transmitted during dialysis underscores

TABLE 2. COMPARISONS OF HUMAN CASES AND DEATHS FROM WNV
(SOURCE: CDC)

Year	Human cases	Deaths
2002	1,201	43
2003	2,923	54
2004	1,386	35
2005	1,299	29



the necessity for dialysis facilities to strictly adhere to proper infection-control procedures at all times (CDC recommendations 2001; see Table 3 for clinical features).

Transmission

In 2002, scientists discovered that the WNV could be spread through blood transfusions and organs/tissue transplants. The risk of getting WNV through these procedures is considered to be quite low. There is evidence that the virus can also be spread through breast milk, and from a pregnant mother to her unborn baby. In addition, laboratory workers who handle specimens with WNV can become infected through needle punctures or small cuts. There is no evidence to suggest that you could get WVN by touching or kissing an infected person, or for being around a health care worker who has treated an infected person. There is no evidence that the virus can pass from infected animals, such horses and pets, to people. However, it is still important to follow standard health and safety practices if you are going to handle dead birds or animals.

Vaccines

The use of DNA-based vaccines is a novel and promising immunization approach for the development of flavivirus vaccines. This approach has been attempted in vaccine development for various virus species, including St. Louis encephalitis, Russian spring-summer encephalitis, Central European encephalitis, dengue serotypes 1 and 2, Murray Valley encephalitis, Japanese encephalitis, and WNV. The use of DNA vaccines is multivalent, and/or combination vaccines designed to immunize against multiple flaviviruses is a promising area of development (White, 2001).

A surprising place to test some of these early vaccines to WNV has become horse stables. The $25 billion horse show and racing industry has begun to suffer greatly from WNV infection. Horses are another favorite source of blood meals for mosquitoes and seem to be especially susceptible to encephalitis. Therefore, the horse industry has strongly supported the creation of a veterinary vaccine for WNV. With luck, a successful vaccine for WNV will serve both horses and humans equally. A vaccine that is economical and easy to distribute provides the best means to protect large populations against the virus, with the fewest undesirable side effects (Sfakianos, 2005).

Treatment

Treatment is supportive, often involving hospitalization, intravenous fluids, respiratory support, and prevention of secondary infections with patients with severe disease.

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TABLE 3. CLINICAL FEATURES OF WNV

Mild infection

Most WNV infections are mild and often clinically unapparent. Approximately 20% of those infected develop a generally mild illness (West Nile Fever).

The incubation period is thought to range 3–14 days.

Symptoms generally last 3–6 days.

Reports from earlier outbreaks describe the mild form of WNV infection as a febrile illness of sudden onset often accompanied by:

- malaise.
- anorexia.
- nausea.
- vomiting.
- eye pain.
- headache.
- myalgia.
- rash.
- lymphadenopathy.

Severe infection

Approximately one in 150 infections will result in severe neurological disease. The most significant risk factor for developing severe neurological disease is advanced age. Encephalitis is more commonly reported than meningitis.

In recent outbreaks, symptoms occurring among patients hospitalized with severe disease include:

- fever.
- weakness.
- gastrointestinal symptoms.
- change in mental status.

A minority of patients with severe disease can develop a maculopapular or morbilliform rash involving the neck, trunk, arms, or legs.

Several patients experience severe muscle weakness and flaccid paralysis.

Neurological presentations can include:

- ataxia and extrapyramidal signs.
- cranial nerve abnormalities.
- myelitis.
- optic neuritis.
- polyradiculitis.
- seizures.

Study: catheter infections could be reduced

A new University of Michigan Health System study found that millions of hospital patients could avoid the risks that come with urinary catheters if hospitals had a system to remind doctors to remove the devices on time.

The study, published in the August issue of *Joint Commission Journal on Quality and Patient Safety*, shows that a written reminder can jog a doctor's memory and lead to patients spending less time with a catheter.

Researchers estimated that the reminder system would cost about $53,200 per year, while average savings in medications and hospital stays would be about $53,449. Sanjay Saint, MD, MPH, lead author of the study, said that if all doctors in a hospital complied with the system, then the savings could be in the tens of thousands of dollars.

The controlled trial took place over 16 months in four wards of U-M's University Hospital, involving patients admitted for surgery or general ailments, including kidney and lung problems. Two wards used the reminder system, and two did not.

The proportion of each catheter patient's hospital stay went down by about 8% in the wards using reminders, and up about 15% in the other wards. Excluding the doctor's who ignored the reminders, the length of stay went down almost 26%.

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