West Nile Virus RNA in Tissues from Donor Associated with Transmission to Organ Transplant Recipients

[Announcer] This program is presented by the Centers for Disease Control and Prevention

West Nile Virus, a mosquito-borne flavivirus, was detected in North America in 1999 and has since become endemic to the United States, where it causes annual seasonal outbreaks. An estimated 70 to 80 percent of human West Nile Virus infections are asymptomatic. Most symptomatic persons experience acute systemic febrile illness; West Nile neurologic disease develops in less than 1 percent of infected persons but has a case-fatality rate of 9 percent. Most West Nile Virus infections are acquired through bites from infected mosquitoes. However, the virus can also be transmitted by transfusion of infected blood products or by solid organ transplantation. In 6 clusters of organ transplant–transmitted West Nile Virus infections reported to public health agencies in the United States, 12 of 16 recipients were infected. Encephalitis developed in 9 of those recipients; 4 of those 9 died.

West Nile Virus transmission through tissue transplantation, for instance, skin, muscle, or connective tissues, has not been identified, and the risk for transmission by this route is not known. We evaluated tissues collected from a deceased donor who was associated with transmission of West Nile Virus through solid organ transplantation to determine if West Nile Virus RNA, viral antigen, or infectious viral particles could be detected in postmortem tissues.

In 2011, the CDC assisted state and local health departments in an investigation of a cluster of West Nile Virus disease transmitted through solid organ transplantation. The adult male donor had a history of cerebral palsy, seizures, and blindness. He was cared for at home and had outdoor exposure in a county with known West Nile Virus activity. In late summer, he had acute onset of fever and lethargy; 2 days after symptom onset, a urinary tract infection was diagnosed, and he received oral antimicrobial drugs. The following day, he suffered cardiopulmonary arrest. After resuscitation, he remained unresponsive, and an electroencephalogram showed no cortical activity. After consent was obtained, solid organs, such as, kidneys, lungs, and liver, and tissues, skin, fat, muscle, tendon, and bone, were procured 9 days after his illness onset. Corneas, heart valves, and vascular tissue were not procured. The donor's organs were transplanted into 4 recipients; none of the donor tissues were transplanted.

After West Nile Virus infection was detected in 1 of the organ recipients 10 days after transplantation, the donor's stored clinical samples, such as serum and spleen/lymph node homogenate, were retrospectively tested for West Nile Virus; this testing occurred within 5 weeks after transplantation. The donor's serum sample was positive for West Nile Virus IgM, IgG, and neutralizing antibodies by serologic testing but negative for West Nile Virus RNA by nucleic acid amplification testing. West Nile Virus RNA was detected in spleen/lymph node homogenate. Subsequently, all 4 organ donor recipients were tested and had positive results for West Nile Virus RNA. Two of the recipients died of West Nile Virus infection.

Five weeks after the donor's death, frozen spleen/lymph node homogenate from the donor that had been used for human leukocyte antigen testing was sent from the transplant center to CDC, and initial West Nile Virus PCR testing was performed as part of the transplant-transmission

investigation. Eight weeks after the donor's death, skin samples that had been treated in cryopreservative solution containing an antibiotic and unprocessed fat, muscle, tendon, and bone samples, all of which had been stored frozen at -70° Celsius at a tissue bank, were transferred to CDC. There, the tissues remained frozen at -20° Celsius to -70° Celsius in individual double-wrapping and plastic bags and were handled and tested separately to reduce the risk for cross-contamination.

West Nile Virus RNA was detected in samples from the spleen/lymph node, skin, and fat associated with the tibia bone, as well as 1 of 2 muscle specimens, 1 of 4 tendon specimens, and 1 of 2 bone marrow specimens. Cytopathic effect was noted only in Vero cells injected with the spleen/lymph node homogenate; these cells were positive for West Nile Virus by RT-PCR, immunofluorescence, and electron microscopy. Cytopathic effect was not observed in Vero cells injected with skin, fat, muscle, tendon, or bone marrow. Results of IHC staining of skin, fat, muscle, and bone marrow samples were negative for West Nile Virus antigens.

We identified West Nile Virus RNA in spleen/lymph node homogenate, skin, fat, muscle, tendon, and bone marrow samples obtained postmortem from a donor associated with transmission of West Nile Virus through solid organ transplantation. West Nile Virus was isolated from the spleen/lymph node homogenate, indicating infectious virus. However, infectious virus could not be cultured, and West Nile Virus antigens were not identified by IHC staining from any of the West Nile Virus RNA-positive tissues.

Data on the detection of West Nile Virus in postmortem organs or tissues are limited. In a study published in 1954, a total of 95 patients with terminal cancer were injected intramuscularly with West Nile Virus. Among 14 patients who died within 1 month after inoculation, virus was isolated postmortem from solid organs in 11 patients and, in 1 patient each, from skin, muscle, or connective tissue. In a more recent study of 6 patients with fatal mosquito-borne West Nile Virus encephalitis, West Nile Virus RNA or antigens were variably detected in solid organ samples from all patients, and West Nile Virus antigens were identified in skin samples from 1 patient. However, 4 of these patients were severely immunocompromised transplant recipients. In 2 of the immunocompetent patients, 1 had West Nile Virus RNA in brain, spleen, and kidney samples and 1 had West Nile Virus antigens only in brain samples. West Nile Virus has also been cultured from an antemortem skin biopsy sample from a patient with rare hemorrhagic manifestations of disease.

Although West Nile Virus RNA was detected in unprocessed tissues obtained from the organ donor, the absence of viral antigen by IHC staining and failure to culture infectious virus from skin, muscle, and tendon suggests that the risk for West Nile Virus transmission may be lower for transplantation of these tissues than for transplantation of solid organs. Further studies are needed to determine if infectious West Nile Virus can be recovered from and possibly transmitted by transplantation of postmortem tissues and, if so, to assess the period of risk and whether tissue processing would mitigate the risk.

This is an abridged version of an EID article, *West Nile Virus RNA in Tissues from Donor Associated with Transmission to Organ Transplant Recipients*, published in the September 2013 issue of *Emerging Infectious Diseases* at cdc.gov/eid

If you would like to comment on this presentation, send an email to eideditor@cdc.gov. I'm William Hale for *Emerging Infectious Diseases*.

[Announcer] For the most accurate health information, visit www.cdc.gov or call 1-800-CDC-INFO.