

# Position statement on West Nile virus: a committee opinion

Practice Committees of the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology

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Although there is currently no definitive evidence linking West Nile virus (WNV) transmission with reproductive cells, it is recommended that practitioners defer gamete donors who have confirmed or suspected WNV infections. This document replaces the previously published document of the same name, last published in 2016 (*Fertil Steril* 2016;105:e9-10). (*Fertil Steril*® 2018;110:e1-3. ©2018 by American Society for Reproductive Medicine.)

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**W**est Nile virus (WNV) is a flavivirus still commonly found in Africa and the Middle East. It is closely related to the St. Louis encephalitis virus, which has appeared in previous limited epidemics in the United States. The primary mode of WNV transmission to humans is through infected mosquitoes (therefore, classified as an arbovirus). The normal transmission cycle for West Nile virus is from mosquito to bird and back to mosquito. The viral load in humans is too low to infect the mosquito and therefore human transmission is considered a termination point in the transmission cycle for West Nile virus (1).

There has been a significant increase in the number of reported cases of WNV infection in the United States over the past 2 decades (2). The first appearance of WNV in North America occurred in 1999, with encephalitis reported in humans and horses. According to the Centers for Disease Control and Prevention (CDC), there were 62 human cases reported from four states and six deaths occurred in 1999. In 2002, there were 4,156 human cases re-

ported from 44 states and the District of Columbia and 262 deaths occurred (2). In 2003, the number of human cases reached 9,858 from 45 states and the District of Columbia with 264 deaths reported (2). In 2009, cases decreased dramatically with only 720 cases of WNV and 32 fatalities reported in the United States with the majority occurring in Colorado, California, and Texas (2). However, case numbers have increased significantly again with 5,674 total cases reported in 2012. Since then, the numbers of cases per year have been consistent in the range of 2,200–2,500 (2).

Approximately 80% of those infected with WNV remain asymptomatic. Approximately 20% develop “West Nile fever,” which typically lasts only a few days and is characterized by a mild illness with flu-like symptoms. Approximately 1 in 150 individuals develops central nervous system (CNS) infection characterized by meningitis, encephalitis, or meningoencephalitis. Nationwide, mortality among those who develop meningoencephalitis is approximately 10%.

After initial infection, the virus accesses lymphoid tissues and becomes widely disseminated. Evidence of WNV has been noted in multiple non-neural tissues, including adrenal gland, heart, kidney, liver, and pancreas.

Between August 28 and October 2, 2002, 15 cases of WNV meningoencephalitis or meningitis were diagnosed and reported to the CDC, having onset within 1 month after transfusion of blood products (3). Among these, the CDC determined that transmission via blood products was “highly likely” in several cases. On September 25, 2002, the CDC reported a case of possible transmission of WNV through organ transplantation (4). In this case, four organ recipients from a single donor all developed clinical WNV infection, and the donor’s blood at the time of organ harvest contained WNV sequences (5–7). On October 4, 2002, the CDC reported a case of possible transmission of WNV through breastfeeding (8). On December 20, 2002, the CDC reported a case of transplacental WNV transmission and fetal infection (9), and two cases of laboratory-acquired WNV infections attributed to percutaneous inoculation (10).

The Food and Drug Administration (FDA) has issued guidance to the blood industry, recommending that a

Received July 10, 2018; accepted July 11, 2018.

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*Fertility and Sterility*® Vol. 110, No. 5, October 2018 0015-0282/\$36.00  
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<https://doi.org/10.1016/j.fertnstert.2018.07.009>

potential blood donor with the medical diagnosis or symptoms suggestive of WNV be deferred until 14 days after the condition is resolved or 28 days from the onset of symptoms, whichever is later (3).

The FDA has cleared two tests to be used as screening tests for WNV (11, 12). The first test, IgM Capture ELISA, reportedly can correctly identify an antibody in up to 90%–99% of WNV disease cases. However, because antibody detection is not always specific, the test is considered presumptive and should be confirmed by further testing (11). The nucleic acid test (NAT) detects the genetic material of the virus, can identify early infection in the donor before antibodies are produced (12), and is recommended for WNV screening (3).

The FDA recommends the use of an FDA-licensed NAT to reduce the risk of transmission from living donors. Because >98.5% of WNV infections in each region of the United States (50 states and the District of Columbia) occur between June 1<sup>st</sup> and October 31<sup>st</sup>, the FDA recommends WNV testing for oocyte and semen donors in the United States from June 1<sup>st</sup> through October 31<sup>st</sup> every year. In the case of a repeat semen donor from whom a specimen has already been collected and tested, and for whom retesting is required, the FDA recommends collection of a specimen for WNV NAT testing at the time of (or within 7 days before or after) the first donation that is recovered within the June 1<sup>st</sup> through October 31<sup>st</sup> testing period, even if an earlier specimen was already collected and tested (13). Due to the increased potential for donors to contract WNV infection from June 1<sup>st</sup> through October 31<sup>st</sup>, the FDA suggests collecting a semen specimen for WNV NAT testing at the time of (or within 7 days before or after) each donation made during this time period. Although this additional testing for subsequent donations is not required, any reactive results must be considered when making a determination of donor eligibility.

Any oocyte or semen donor whose specimen tests negative (or nonreactive) for WNV NAT should be considered to be negative (or nonreactive) for WNV for purposes of making a determination of donor eligibility. Any oocyte or semen donor whose specimen tests positive (or reactive) for WNV in the preceding 120 days must be considered ineligible to donate.

This recommendation for testing does not apply to cells and tissues for autologous use such as reproductive cells or tissue donated by a sexually intimate partner, or to cryopreserved cells or tissue for reproductive use that were originally exempt from the donor eligibility requirements. These recommendations by the FDA should be implemented as soon as feasible and should be considered recommendations and not requirements.

It is acknowledged that there are significant limitations with symptom screening for WNV. These include the high incidence of asymptomatic cases as well as the fact that symptoms typically follow the viremic period (the time period presumably most associated with transmission risks).

Despite the recent introduction of WNV screening tests, a number of factors, including test characteristics (sensi-

tivity, specificity, positive predictive value, negative predictive value), anticipated clinical benefits, and costs, need to be carefully evaluated before any global recommendations for WNV testing in reproductive medicine can be offered.

## SUMMARY

- The FDA recommends WNV screening for oocyte and semen donors in the United States from June 1<sup>st</sup> through October 31<sup>st</sup> every year using NAT because >98.5% of WNV infections in each region of the United States (50 states and the District of Columbia) occur between June 1<sup>st</sup> and October 31<sup>st</sup>.
- Although there is currently no definitive evidence linking WNV transmission with reproductive cells, it is recommended that practitioners defer gamete donors who have confirmed or suspected WNV infections in the preceding 120 days.

## CONCLUSION

- Good donor practice would suggest that donors who are not in good health, including those with recent significant fever and flu-like illnesses, as well as those with recent viral meningitis, encephalitis, or meningoencephalitis episodes, be similarly deferred.

**Acknowledgments:** This report was developed under the direction of the Practice Committee of the American Society for Reproductive Medicine as a service to its members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations. The Practice Committee and the Board of Directors of the American Society for Reproductive Medicine have approved this report.

This document was reviewed by ASRM members and their input was considered in the preparation of the final document. The Practice Committee acknowledges the special contribution of Sangita Jindal, PhD and David Ball, PhD in the preparation of this document. The following members of the ASRM Practice Committee participated in the development of this document. All Committee members disclosed commercial and financial relationships with manufacturers or distributors of goods or services used to treat patients. Members of the Committee who were found to have conflicts of interest based on the relationships disclosed did not participate in the discussion or development of this document.

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