OPTN Ad Hoc Disease Transmission Advisory Committee
Require West Nile Virus (WNV) Seasonal Testing Workgroup
Meeting Summary
December 18, 2024
Conference Call

Stephanie Pouch, MD, MS, Chair
Rachel Miller, MD, Vice Chair

Introduction

The OPTN Require West Nile Virus Seasonal Testing Workgroup (the workgroup) met via WebEx teleconference on 12/18/2024 to discuss the following agenda items:

1. Project Overview: Background & Purpose
2. West Nile Virus Presentation

The following is a summary of the Committee's discussions.

1. Project Overview: Background & Purpose

The purpose of this project is to require West Nile Virus (WNV) testing for living and deceased donors to improve patient safety for solid organ transplant recipients by reducing unintended WNV disease transmission and deaths.

This project is a request from the Center for Disease Control and Prevention (CDC) to consider West Nile Virus (WNV) testing requirements consistent with CDC and the Food and Drug Administration (FDA) recommendations.

The workgroup project will be a collaborative effort between representatives from the CDC, FDA, and Organ Procurement and Transplant Network (OPTN) Committees, including, the sponsoring committee, Ad Hoc Disease Transmission Advisory Committee, Organ Procurement Organization (OPO), and the Living Donor Committee.

2. West Nile Virus Presentation

The Workgroup heard a presentation on West Nile Virus Transmission by Solid Organ Transplantation by CDC representatives.

The workgroup was asked to determine the optimal WNV screening assay(s) for donor screening based on:

- Test performance
- Assay availability
- Timing of results

<u>Data summary:</u>

WNV is the leading cause of domestic arboviral disease spread by Culex species mosquitos. Since 1999, there have been more than 59, 000 human disease cases and more than 2900 deaths. There is currently

no treatments or human vaccines available.[1] Based on CDC investigation and review of literature summarized showed that since 2002, there have been 11 confirmed clusters of those 26 out of 30 (87%) involved recipients that had evidence of WNV infection. Of those infected, 20/26 (77%) developed encephalitis. Of those who developed encephalitis 8/20 (40%) died.[2]

Of this investigation, only 1/11 were screened for WNV. 10 of the donors were not screen and on retrospective testing, 7 were positive for viremic. Screening could have prevented at least 7 transmission events. WNV is seasonal and most disease cases that are reported are between June through October.

Based on surveys that have been conducted, studies showed that a majority of deceased organ donors were not screened for WNV at Organ Procurement Organizations (OPO). In 2019, 46/47 OPOs were survey, and of those, 18 (39%) indicated that they performed WNV screening. Most of the OPOs surveyed indicated they did year-round WNV screening, while 1 indicated that they performed seasonal WNV screening.[3]

<u>The Food Drug and Administration (FDA) recommendations for WNV screening of blood donations</u>

The FDA recommends year-round screening using licensed Nucleic Acid Testing (NAT)

- Minipool (MP) or individual donation (ID) testing
- Switch to ID –NAT during high WNV activity in specified region using defined threshold.

Presumptive viremic donation (PVD) criteria lead to high positive predictive value

The two types of assays used include:

- Transcription –mediated amplification (TMA)
    - If the center is using TMA, they must have a WNV initially reactive donation with signal to cutoff ratio greater or equal to 17 OR
    - Repeat test reactive
- Real-Time Reverse Transcription (RT) Polymerase Chain Reaction (PCR)
    - WNV initially reactive donation if repeat test reactive
    - Less than or equal to 95% of PVDs as defined are confirmed by additional testing (low false positive rate)

<u>Limitations to WNV screening</u>

- Sensitivity and specificity in organ donors known
    - Potential false negatives (e.g., hemodilution, organ sequestration)
    - Potential false positive (using PVD criteria could mitigate this)
- Laboratory and staff resources
- Need for timely results
- WNV activity variable and unpredictable from year to year

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[1] Center for Disease Control and Prevention. "Historic Data (1999 – 2023)." https://www.cdc.gov/west-nile-virus/data-maps/historic-data.html (Accessed February 4, 2024). https://www.cdc.gov/west-nile-virus/data-maps/historic-data.html

[2] Sutter RA, et al. West Nile Virus and Other Nationally Notifiable Arboviral Diseases- United States, 2022. May 30, 2024. 73(21);484–488. ((Accessed February 4, 2024).

[3] Nett RJ et al. Transpl Infect Dis 2012;14:268–77 Theodoropoulos NM. Am J Transplantation 2021;21:1924–30

Summary of discussion:

The Chair stated that the workgroup would like to determine the optimal WVN screening assays and approaches for deceased and living donors. These considerations include test performance, availability, and timing of results. Historically there are multiple approaches to screening. She highlighted that universal year-round screening comes with challenges, including organ nonuse if donors are screened outside an endemic area. Also, trigger testing can be logistically challenging and does not take into account previous movement of the donor prior to donation. Therefore, a seasonal approach seems to be the best approach to donor screening within a predetermined time period. Based on the presentation and recommendations from the CDC, nucleic acid testing in a predefined seasonal period could be considered for testing donors for WNV. There are concerns with immunoglobulin M (IgM) test performance and the potential for false positive results. Regarding the timing of results, results are needed prior to organ transplantation because no treatment is available for WNV.

Regarding the 18 OPOs that screen for WNV, a member asked about the number of cases they have detected. A member shared that their OPO adopted WNV screening in 2005, and there are about 350 donors a year and an additional 200 tests that are performed on patients who end up not being donors for one reason or another. The member stated that there may not have ever been a positive WNV test result. He further explained their process is straightforward, as their OPO has an infectious disease screening lab, and the cost is around $25 per donor. This OPO conducts year-round WNV screening, noting that seasonal screening could be risky since someone might forget to request the test around July 1st. The member emphasized that the test is easy and low-cost, so year-round screening works best at their OPO.

Regarding the minipool test vs. ID test, a member asked if the workgroup would only consider ID NAT. The Chair confirmed that they would consider ID NAT.

On the topic of seasonal versus year-round WNV testing, a member stated that seasonal testing may be logistically challenging, so it would be best to get input from the labs. A CDC representative clarified that "seasonal" refers to donors recovered between July 1st and October 31st would be subject to WNV testing, so it's not truly seasonal but rather several months of the year. Another member provided additional context, explaining that over time, the OPOs have faced increasing costs for various infectious disease screenings required for all donors, including toxoplasmosis, strongyloidiasis, and Chagas for individuals born in an endemic country. Adding another test, like WNV, is an additional cost burden for OPOs. The member suggested trying to strike a balance between risk and cost, focusing the testing on the timeframe when transmissions and positivity are most likely.

Another member commented that WNV is performed on all living donors year-round at her living donor program. At one time, their program was conducting WNV seasonal testing, but it can be subjective at times. Also, many living donors may be well-traveled and might be traveling to endemic areas. As it relates to living donors, tighter guidelines and less ambiguity is helpful. She further shared that at her program, there are local donors who donate at other centers, such as California or Arizona, where they are doing a lot more endemic infectious disease testing, and these donors have had incidental positive tests, which their program had to address. The member suggested the workgroup consider both endemic and North American perspectives as they develop testing recommendations.

Another member stated when testing deceased donors, there can be false positives, which may result in a loss of organs; it may be more reasonable to do testing on a seasonal basis. Another member asked what the rate for false positive NAT testing is. A CDC representative responded that there is no information anecdotally of false positives being identified. It would be worth collecting this information from OPOs who have done screening to understand how many positives they've identified over the years.

The Chair summarized that the workgroup seems to favor a NAT-based testing recommendation due to the uncertainty around positive serologic testing, particularly the IgM. The workgroup would also like to consider a defined seasonal testing period, rather than year-round screening.

Finally, a member asked about the turnaround time for NAT testing, and another member responded that it usually takes 8 hours or less. The Chair stated that the testing is not expected to prolong donor evaluation management times significantly.

Upcoming Meetings

- TBD

Attendance

- **Committee Members**
    - Shirish Huprikar
    - PJ Geraghty
    - Anna Hughart-Smith
    - Dong Lee
    - Gabriel Maine
    - Anni Doyle
    - Lara Danziger-Isakov
    - Rachel Miller
    - Stephanie Pouch
    - Fernanda Silveria
    - Tanvi Sharma
    - Kerri Jones
- **HRSA Representatives**
    - Marilyn Levi
- **FDA Representatives**
    - Brychan Clark
- **CDC Representatives**
    - Sridhar Basavaraju
    - Pallavi Annambhotla
    - Carolyn Gould
- **SRTR Staff**
- **UNOS Staff**
    - Tamika Watkins
    - Susan Tlusty
    - Cole Fox
    - Logan Saxer
    - Laura Schmitt
- **Other Attendees**