Zika Virus and Risk of Donor Transmission

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On behalf of the OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC)
Zika virus and Organ Transplantation: Questions

- What are the consequences of Zika virus in transplant recipients or other immunosuppressed hosts?
- How long does infectious Zika virus persist in different organs?
- Will testing be appropriate and practical for potential organ donors?
- Are there recommendations that can be made in interim?
Ad Hoc Disease Transmission Advisory Committee (DTAC)

- Part of OPTN patient safety program
- Examine unexpected potential donor-derived transmission events mainly consisting of infection or malignancy
  - Categorize as to whether or not they are donor derived
- Evaluate aggregate data to enhance patient safety
  - Inform policy change and improve existing processes
  - Educate transplant community
Potential Donor Derived Transmission Events (PDDTE)

Number of PDDTE Reviewed by DTAC*, 2005-2015

*Additional reports are submitted, but not reviewed by full DTAC (duplicates, expected transmissions and other unnecessary reporting, etc).

Kaul et al ATC 2015
Zika Virus and Transplantation

What do we know so far?

- Thus far, organ donor-derived transmission has not been reported
  - 2015-16: 488 cases submitted to DTAC and none with Zika virus

- Literature: 3 HIV + people with Zika virus, without significant disease

- Other flaviviruses have been transmitted with donor organs

- West Nile Virus (WNV) well recognized to be donor transmitted with more severe consequences compared to WNV in healthy hosts

- Anecdotal case reports of dengue transmission in endemic countries
Zika virus and Immunosuppressed Patients: Potential for Infection

- Zika virus found in blood, bodily fluids and tissues

- 2013: French Polynesia outbreak: 42/1505 (3%) blood donors test (+)
  - European Communicable Disease Bulletin. 19(14), 2014

- 2016: 1% of asymptomatic blood donors in Puerto Rico test (+)
  - Kuehnert MJ et al. MMWR 2016; Jun 2; 65; 627-8

- Brazil: Several transfusion associated cases
  - Genome Announcements March/April 2016
  - Barjas-Castro et al. Transfusion 2016; 1684
Recipient asymptomatic
Day 18 follow up: Ab + against Flavivirus still
99.8% homology in the sequenced sections of blood donor and recipient virus

- Accordingly, platelet transfusion suspected as the culprit

While anecdotal, reassuring that liver recipient asymptomatic despite infection on day of transplant

- Cleared viremia on day 18 sample

Recognition of case was dependent on the blood donor reporting symptoms 2 days after donation
FDA Guidance for Industry
Recommendations - Blood Donors

- February 10, 2016
- Defer for 4 weeks:
  - After resolution of symptoms if diagnosed with Zika virus
  - If travel to area with Zika virus transmission
  - After last sexual contact with a man with Zika virus exposure or Zika virus in past 3 months
Guidance for Industry

- Blood banks with locally acquired mosquito-borne cases of Zika virus should be testing: FL and PR
- Neighboring states or those with other epidemiological linkage to Zika virus should implement testing within 4 weeks: AL, AZ, CA, GA, HI, LA, MS, NM, NY, SC, TX
- All others implement as soon as feasible but not later than 12 weeks
- Ok to use investigational ID-NAT under IND or FDA approved pathogen reduction
Guidance for Industry

• Blood donors who test (+) should be informed and counseled
  • Defer further donation for 120 days from positive test or symptom resolution (whichever is longer)
• If blood components had been used, the recipient’s physician should be notified
Living donors

- Ineligible if in past 6 months
- Zika virus diagnosis
- Travel to areas with active Zika virus in past 6 months
- Sex in past 6 months with male partner with either of the above

Non-heart beating cadaveric donors of HCT/Ps

- Ineligible if medical diagnosis of Zika virus in past 6 months
Guidance for Living Donation

Working together. Saving lives.

UNOS Transplant Pro

recipient. Other travel related conditions should also be considered; the same vector that transmits Zika virus, A. aegypti, also transmits dengue and chikungunya viruses.

Although the CDC guidance on pregnancy did not specifically address organ donation to pregnant women or women of child-bearing age, donor deferral should be considered if there is history of travel to Zika-endemic areas in the 28 days prior to donation. In the case of potential living donors with Zika infection, donation should be deferred where possible.

Things for Transplant Centers to consider when discussing travel with patients:
For patients who are either pre or post-transplant and wish to travel to areas endemic for Zika virus, standard travel precautions are advised. These include seeking expert advice from a Travel Medicine clinic or Infectious Disease physician, as well as routine counselling on preventative measures such as mosquito avoidance.

Where has Zika virus been found?
See CDC maps showing countries and territories with active Zika virus transmission.

Things for OPOs and Transplant Centers to consider when evaluating potential organ donors:
OPOs should focus on recent travel history and epidemiologic risk factors, as well as recent donor symptoms (although only about 20% of infected individuals will be symptomatic), and highlight this information when organ offers are made. While infected potential donors may possibly transmit Zika virus to recipients, DTAC, AST, and ASTS do not believe concern for Zika virus infections should summarily exclude donors from transplantation; rather, the risk of donor derived infection should be balanced with the benefits of transplantation in each potential recipient. Other travel related conditions should also be considered; the same vector that transmits Zika virus, A. aegypti, also transmits dengue and chikungunya viruses.

Learning from Experience: LifeLink of Puerto Rico

<table>
<thead>
<tr>
<th>San Juan Donor Activity</th>
<th>January-August 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ Donors</td>
<td>61</td>
</tr>
<tr>
<td>Organs Transplanted</td>
<td>191</td>
</tr>
<tr>
<td>• Local (Auxilio Mutuo)</td>
<td>88</td>
</tr>
<tr>
<td>• Exported (Mainland)</td>
<td>103</td>
</tr>
</tbody>
</table>
Zika Virus Documentation Rationale
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Revised: 02/09/16 - Implemented: 02/09/16

LifeLink Organ Procurement Organization

Zika Virus Documentation Rationale

The following will be documented regarding the Zika virus on donors where organs are intended and allocated for transplant by LifeLink. This information will be documented in DonorNet (Donor Highlights) when offering organs for transplant:

LLPR – “As reported by the CDC, Puerto Rico is a Zika endemic area”

LLFL and LLGA – “This donor has traveled to XXX within the last 28 days. According to the CDC, XXX is a Zika endemic area.”

Guidance provided by OPTN/UNOS Ad Hoc Disease Transmission Advisory Committee (DTAC), the American Society of Transplantation (AST), and the American Society of Transplant Surgeons (ASTS), after careful review of information available from the Centers for Disease Control and Prevention (CDC) is posted below.
Addendum Implemented

Implement March 28, 2016
Zika Virus (ZIKV) Questionnaire

Z2. Did she/he recently have any symptoms such as:
   Z2a. Joint pain? □ No □ Yes

   Z2b. Conjunctivitis, which is also called "pink eye" or "red eye"?
        □ No □ Yes

   Z2b(1). When? ______________________

   Z2b(2). Describe the conjunctivitis and ______________________

Z3. Describe any of her/his travel to a Zika Virus active transmission area within the past 6 months.
   □ No travel to Zika Virus active transmission areas

   References question #10 on the LifeLink Confidential Donor Medical History and Behavioral Risk Assessment Questionnaire
Prevention

How can I protect myself from MOSQUITOES?
Safe Living Before and After Transplantation Advice for Candidates and Recipients:

- **Living in Zika virus active transmission area:**
  - Use protective measures to avoid mosquito bites & avoidance of sex or use of condoms with sex with males

- **Not living in area with active Zika virus transmission**
  - Travel precautions should be discussed including Risk : Benefit
  - IF traveling:
    - Avoidance of sex or correct condom use with sex with males
    - Standard mosquito avoidance measurements including 3 weeks post return
      - Repellant, long sleeved shirts & pants, treated clothes, air-conditioning, screens and nets

Living Donors:
Still with questions

- What is an appropriate period for deferral if diagnosed with Zika virus or symptoms suggestive of Zika virus?

- How should we counsel potential donors regarding
  - Travel to areas of Zika virus activity in the pre-donation period?
  - Sexual contacts with males who traveled to endemic areas?
  - Living in area with Zika virus activity?
Where are we and Where to go from here

- Recognize potential for transmission of Zika virus
- Low threshold for evaluation of recipients with symptoms
- Report suspected Zika virus transmission due to transplantation
- Continue to encourage living donors to report post-donation symptoms
- Learn from centers and sites where Zika virus currently active
Future Challenges: Zika transmission in the continental USA

- Rapidly changing epidemiology
- Definitely a problem during pregnancy
- Still unknown if a problem for transplantation
- Better understanding needed:
  - Disease in the transplant recipient
  - Risk of transmission via donor organ
- Lab logistics and challenges
- Development of treatment strategies
The need continues to grow
Every ten minutes, someone is added to the national transplant waiting list. On average, 22 people die each day while waiting for a transplant.
Risk-benefit analysis
Reality and perception of risk

Courtesy of Dr Tim Pruett
RESOURCES

- NYSDOH Zika Info Line & website
  888-364-4723 (M-F 9AM-5PM)


  https://optn.transplant.hrsa.gov/resources/patient-safety
RESOURCES

- FDA
  http://www.fda.gov/Emergencypreparedness/Counterterrorism/Medicalcountermeasures/MCMIssues/ucm485199.htm


- NYC DEPARTMENT OF HEALTH AND MENTAL HYGIENE-NYCDOHM
  http://www1.nyc.gov/site/doh/providers/reporting-and-services.page
  NYCDOHM Provider Access Line: 1 (866) 692-3641
QUESTIONS

NYSDOH Zika Information Line:
1-888-364-4723
Monday to Friday, 9 am to 5 pm

NYSDOH contact- Lisa McMurdoo
 lisa.mcmurdo@health.ny.gov