Risk of Other Donor-Derived Infections (nonHIV, nonHCV)

Daniel Kaul MD
Associate Professor
University of Michigan
Conflict of Interest Disclosure

- I have no relevant financial relationships to disclose
- No off-label use will be discussed
Topics

• Clinical donor evaluation
• Bacterial infection
• Geographically/seasonally restricted infections
• Zika virus
Donor derived disease (DTAC reports)

• Vast majority of reports involve pathogens other than viral hepatitis and HIV
• Malignancy
  – 55 recipients with 26 deaths
• Fungal infections
  – 41 recipients with 13 deaths
• Bacterial infections
  – 49 recipients with 8 deaths
• Parasite/amoeba
  – 31 recipients with 10 deaths
• CNS pathogens
Donor Screening Tests for Selected Situations

- Site specific protocols are used
- **West Nile virus nucleic acid amplification testing**
  - During periods of increased mosquito activity or known outbreaks
- **Trypansoma cruzi** (serology)
  - At-risk donors
- **Coccidiomycosis** (serology)
  - Southwestern states
- **Strongyloides** (serology)
- **Human T-cell lymphotropic virus (HTLV-1)** (serology)
  - At-risk donors
Considerations when Evaluating Organs from Donors with Possible Infection

• Has the infection been identified, and is effective treatment available?
  – Pneumococcal meningitis

• Is the cause of presumed infection unknown?
  – Encephalitis of unknown cause

• Is it a multidrug resistant organism?
  – Toxicity and poor efficacy of available treatment options

• What is the extent of the infection?
  – Septic shock with multiple organ involvement
Case

• Potential donor: male with injection drug use
  – MRSA bacteremia
  – Septic emboli to brain
  – Afebrile, on antibiotics for more than 48 hours

• Recipient critically ill
  – End stage pulmonary fibrosis
  – Mechanical ventilation in ICU

• Should organs from this donor be transplanted?

MRSA: Methicillin-resistant Staphylococcus aureus
ICU: Intensive care unit.
Outcome of Recipients of MRSA Endocarditis Donor

- Lungs, liver, kidneys, and pancreas transplanted

- Prophylaxis given to all recipients

- Liver and lung recipient with recurrent MRSA

- Both infected recipients doing well > one year after transplant
Donors with bacteremia or endocarditis

• About 5% of donors have bacteremia at procurement
• Outcomes good
  – Recipient and donor treated
  – Not an MDR organism
  – Typically treat recipients for 7 days
• Donors with endocarditis
  – One publication with 5 donors with good outcomes
  – 4/5 with coagulase negative staph, one with enterococcus
  – MRSA and other more virulent organisms; exercise caution

Multi-drug resistant gram negative infections

- Gram negative resistance growing problem
- Donor with open abdomen
- Death may occur even with appropriate treatment
- Treatment may be toxic

Figure 2: Outcome of recipients at high risk of MDR transmission (recipients who received organs from donors with BSI or with an infection at the same transplanted organ site) based on appropriateness, timing of initiation, and duration of targeted antibiotic treatment. MDR, multidrug-resistant; BSI, bloodstream infection.

### Endemic infections may present later after transplant

<table>
<thead>
<tr>
<th></th>
<th>0-30 days</th>
<th>31-90 days</th>
<th>91-180 days</th>
<th>&gt; 180 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral</td>
<td>LCM</td>
<td>CMV (3)</td>
<td>Hepatitis C</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td>WNV (4)</td>
<td>Parvovirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>RSV</td>
<td>WNV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial</td>
<td>Assorted (23)</td>
<td>Klebseilla</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fungal</td>
<td>Candida (3)</td>
<td>Aspergillus</td>
<td>Aspergillus</td>
<td>Aspergillus</td>
</tr>
<tr>
<td></td>
<td><strong>Coccidioides</strong> (6)</td>
<td>Coccidioides (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aspergillus</td>
<td><strong>Histoplasmosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cryptococcus (4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Scopulariopsis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zygomycete (2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycobacterial</td>
<td>M. tuberculosis (2)</td>
<td>M. tuberculosis (2)</td>
<td>M. tuberculosis (2)</td>
<td></td>
</tr>
<tr>
<td>Parasitic</td>
<td>Toxoplasma</td>
<td>Strongyloides</td>
<td>Strongyloides (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Balamuthia (5)</td>
<td>Toxoplasma</td>
<td>Toxoplasma</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Encephalitozoon (2)</td>
<td>Encephalitozoon Balamuthia</td>
<td></td>
</tr>
</tbody>
</table>

Kaul et al/ ATC 2013
Transmission of Coccidioidomycosis through Organ Transplantation

Recipient Mortality at 4 months

- 6 proven or probable cases 2008-2012
- 9/21 recipients infected
- Dx median 30 days
- 6 deaths median 21 days post tx

Kusne1, S Taranto2, S Covington2, D Kaul1, W Bell1, SW Biggins1, E Blumberg1, GD DeStefano1, E Dominguez1, D Ennis1, M Klassen-Fischer1, C Kotton1, Y Law1, M Menegus1, R Miller1, M Pavlakis1, TL Pruett1, D LaPointe Rudow1, P Ruiz1, N Siparsky1, M Souter1, L Weiss1, C Wolfe1, and M Green1. 1OPTN Ad Hoc Diseases Transmission Advisory Committee. 2United Network or Organ Sharing ATC 2013 Seattle
Coccidioomycosis

- 2.1% of donors in endemic region seropositive
- Serologic screening considered in endemic areas
- Infected living donors
  - Defer donation until after treatment complete and symptoms resolved
- Infected deceased donors
  - Anti-fungal prophylaxis
  - Duration
    - 3-6 months (non-lung)
    - Consider life-long (lung)

Blair JE, Mulligan DC. Coccidioidomycosis in healthy persons evaluated for liver or kidney donation. Transpl Infect Dis 2007
Donor-derived Histoplasmosis

• 8/152 possible DDI
  – Dx first month post-tx
  – Granuloma in tx organ + dx first year post-tx

Transmission of *Histoplasma capsulatum* by Organ Transplantation

Ajit P. Limaye, M.D., Patricia A. Connolly, M.S., Manish Sagar, M.D., Thomas R. Fritsche, M.D., Ph.D., Brad T. Cockson, M.D., Ph.D., L. Joseph Wheat, M.D., and Walter E. Stamm, M.D.

- Azole prophylaxis of recipients of infected donors (3-12 months)
- Serial antigen monitoring
  - Donor with granuloma and comp fix < 1:32 and negative immunodiffusion

American Journal of Transplantation 2012; 12: 2414-2428
Limaye et al, NEJM 343:16 2000
Donor-derived Histoplasmosis

- Less common than Coccidiomycosis
- “routine” serologic screening not indicated

Chagas disease

• 52 year old man received deceased donor renal transplant
• Donor in U.S. for 12 years
• Immigrated from Ecuador
• Testing at CDC sent by tissue bank (processing heart valve) positive serology for Chagas
• What to do for our renal transplant recipient?
Chagas in blood donors

http://www.aabb.org/Content/Programs_and_Services/Data_Center/Chagas
Management of recipient from Chagas positive donor

- Risk of transmission (likely 25-33%)
- Serial PCR (CDC)
  - Weekly for 2 months
  - Every 2 weeks for 3rd month
  - Monthly for 6 months then?
- Treat positive with nifurtimox or benznidazole (CDC)
• 2 recipient deaths
• Donor infection/disease can be prevented with ivermectin
• Worldwide distribution but uncommon in donors without significant residence outside of the U.S.

### Table 1: Donor demographics and characteristics in CDC investigations of *Strongyloides* infection in United States, 2009–2013

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Year</th>
<th>State</th>
<th>Age/Sex</th>
<th>Birth country</th>
<th>Duration of US residence (years)</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2009</td>
<td>NY</td>
<td>55/M</td>
<td>West Indies</td>
<td>21</td>
<td>Head trauma in motor vehicle accident (MVA)</td>
</tr>
<tr>
<td>2</td>
<td>2009</td>
<td>NV</td>
<td>56/F</td>
<td>Honduras</td>
<td>Unknown</td>
<td>Respiratory failure due to asthma exacerbation</td>
</tr>
<tr>
<td>3</td>
<td>2010</td>
<td>PA</td>
<td>54/M</td>
<td>Dominican Republic</td>
<td>2.5</td>
<td>Head trauma secondary to gunshot wound (GSW)</td>
</tr>
<tr>
<td>4</td>
<td>2011</td>
<td>MA</td>
<td>46/M</td>
<td>Honduras</td>
<td>7</td>
<td>Trauma in MVA</td>
</tr>
<tr>
<td>5</td>
<td>2012</td>
<td>NY</td>
<td>45/M</td>
<td>Guyana</td>
<td>14</td>
<td>Cardiac arrest, subarachnoid hemorrhage</td>
</tr>
<tr>
<td>6</td>
<td>2012</td>
<td>FL</td>
<td>49/M</td>
<td>United States</td>
<td>Unknown</td>
<td>Subdural hematoma</td>
</tr>
<tr>
<td>7,10</td>
<td>2012</td>
<td>PA</td>
<td>24/M</td>
<td>Puerto Rico</td>
<td>8</td>
<td>Head trauma secondary to GSW</td>
</tr>
</tbody>
</table>

Donor-derived West Nile Virus

**RECIPIENT DISEASE**
- 70% with neuroinvasive disease
- 30% severe morbidity and mortality
- 5-37 days to onset
- Donor testing not sensitive

**TABLE 2.** Characteristics of published organ donors transmitting WNV infection

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of donors</td>
<td>8</td>
</tr>
<tr>
<td>Age Mean (range), yr</td>
<td>46 (18–78)</td>
</tr>
<tr>
<td>Median (range), yr</td>
<td>43 (18–78)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
</tr>
<tr>
<td>Not reported</td>
<td>1</td>
</tr>
<tr>
<td>Mode of WNV acquisition</td>
<td></td>
</tr>
<tr>
<td>Mosquito</td>
<td>6</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>2</td>
</tr>
<tr>
<td>Residence in area of increased WNV activity</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>Medical condition leading to organ donation</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>4</td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>2</td>
</tr>
<tr>
<td>Gunshot wound</td>
<td>1</td>
</tr>
<tr>
<td>Cerebral palsy, febrile illness</td>
<td>1</td>
</tr>
<tr>
<td>WNV testing before donation</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7</td>
</tr>
<tr>
<td>Yes*</td>
<td>1</td>
</tr>
<tr>
<td>Retrospective WNV testing*</td>
<td></td>
</tr>
<tr>
<td>Positive serum PCR</td>
<td>4/8</td>
</tr>
<tr>
<td>Positive serum IgM</td>
<td>3/8</td>
</tr>
<tr>
<td>Positive serum IgG</td>
<td>4/6</td>
</tr>
<tr>
<td>Positive tissue PCR (lymph node, spleen)</td>
<td>1/1</td>
</tr>
</tbody>
</table>

* Tested negative by NAT, nucleic acid amplification.

* No. of donors positive/No. of donors tested.

WNV, West Nile virus; PCR, polymerase chain reaction.

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# WNV screening tests

## Table 2: Tests that could be used to screen for WNV infection

<table>
<thead>
<tr>
<th>Available Tests</th>
<th>Nucleic Acid Tests (NAT)(^{(1)})</th>
<th>IgM (serology)(^{(2)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procleix West Nile Virus Assay</td>
<td>COBAS TaqScreen West Nile Virus Test</td>
<td>various</td>
</tr>
<tr>
<td>FDA licensed for organ screening</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Availability</td>
<td>Blood bank testing labs</td>
<td>Reference labs</td>
</tr>
<tr>
<td></td>
<td>Reference labs</td>
<td>State Health Departments</td>
</tr>
<tr>
<td>False positive rate</td>
<td>Low</td>
<td>Likely higher than NAT, but not evaluated for donor screening</td>
</tr>
<tr>
<td>Indicates active infection</td>
<td>Yes</td>
<td>Remains positive for median of 5 months; active infection may have cleared</td>
</tr>
<tr>
<td>Required for blood donor screening</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

\(^{(1)}\) Should be used as part of any testing strategy  
\(^{(2)}\) Consider in combination with NAT testing but will increase false positive rate


Zika virus

• No proven or probable cases of donor derived infection in US with Zika, Dengue, Chikungunya
• Routine donor testing not practical
• Blood products (US) and living donors (UK) deferred 28 days from travel
• ASTS/AST/DTAC guidance

Summary

- Most donors with bacteremia or bacterial meningitis can be used
- Caution with MDR bacterial infections
- Preventative strategies available for donors with most seasonal/geographically limited infections
- Zika virus-more questions than answers