Unusual Donor Derived Transplant-associated Infections: Just How Unusual?
Federal Oversight of Organ Procurement and Transplantation

Robert Walsh
Director, Division of Transplantation
Health Resources and Services Administration
Organ Transplant Supply and Demand

http://optn.transplant.hrsa.gov
National Organ Transplant Act, 1984

- Established the Organ Procurement and Transplantation Network (OPTN)
  - Network to be operated by private, nonprofit organization under federal contract with HHS and HRSA
- United Network for Organ Sharing (UNOS) operates the OPTN
- Created the current system of organ procurement organizations (OPOs)
  - Currently 58 OPOs certified by Centers for Medicare and Medicaid Services

HRSA: Health Resources and Services Administration
Structure, membership and oversight function

Goals and requirements for policy making, particularly allocation of organs
  - Waitlist of potential recipients
  - Matches potential recipients with organ donors
  - Donor testing
  - Organ packaging and labeling

Data collection and dissemination on pre-transplant and post-transplant events

Advisory Committee on Organ Transplantation

CFR: Code of Federal Regulations
HIV Organ Policy Equity (HOPE) Act

- HOPE Act signed by US President into law November 21, 2013

- Stipulates that the OPTN may develop standards for use of organs from HIV–positive donors for transplant in individuals who were already infected with HIV
Required Donor Screening Tests for Infectious Pathogens

Deceased Donors

- Hepatitis B surface antigen and core antibody
- Hepatitis C serology, including
  - Hepatitis C nucleic acid amplification testing (NAT) (all donors)*
- HIV antibody
- HIV NAT or 4th generation EIA for donors with increased risk*
- Syphilis
- Cytomegalovirus serology (CMV)
- Epstein-Barr virus serology (EBV)
- Blood culture
- Urine culture

* Pending United Network for Organ Sharing (UNOS) board approval November 2014

EIA: Enzyme immunoassays.
Typical Questions in Deceased Donor Risk Assessment Interview

- Public Health Service criteria for increased risk for incident hepatitis B, hepatitis C, and HIV
  - Sexual exposures, drug use, hemodialysis, inmate of correctional facility, or recent sexually transmitted disease
- Country of origin and previous residence and travel
- General medical history and medications
  - Recent symptoms, including cough, fever, weight loss or headache
- Human growth hormone exposure for CJD risk
- Animal exposures
  - Screening for rabies and lymphocytic choriomeningitis virus

CJD: Creutzfeldt-Jakob Disease
http://www.publichealthreports.org/issueopen.cfm?articleID=2975
Current Waitlist by Organ and Age of Candidate

http://optn.transplant.hrsa.gov/converge/latestData/rptData.asp
Transplants by Organ and Age of Candidate in 2013

http://optn.transplant.hrsa.gov/converge/latestData/rptData.asp
Consequences of the Disparity Between Supply and Demand

- Wait times vary significantly based on severity of illness and other factors

- Median national waiting time
  - For kidney – nearly 4 years
  - For liver – nearly 1.5 years

- In 2013
  - 6,324 transplant candidates died waiting for an organ
  - 4,915 transplant candidates became too sick to transplant

http://optn.transplant.hrsa.gov/converge/latestData/rptData.asp
Current Screening of Organ Donors for Donor-derived Infections

Daniel Kaul, MD
Director, Transplant Infectious Disease Services
University of Michigan
Chair, Disease Transmission Advisory Committee (DTAC)
Donor Screening Tests for Selected Situations (not required)

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

- Severity of disease in recipient affects urgency of need
  - Kidney disease rarely requires urgent transplant
  - High score on MELD is an indication for urgent liver transplant

Estimated 3-month Survival As A Function of MELD Score

MELD: Model for End Stage Liver Disease
http://www.unos.org/docs/MELD_PELD.pdf
Other Considerations of Accepting 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
An Example of High Risk Donor
MRSA Endocarditis in Donor

- **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 doing well, without infection more than one year after transplant

MRSA: Methicillin-resistant Staphylococcus aureus
Monitoring Recipients for Post-transplant Infection and Donor-derived Disease

- Post-transplant formal monitoring system limited to
  - Only HIV, HBV, and HCV

- For other diseases, high index of suspicion needed

---

**PHS Guideline for Reducing Human Immunodeficiency Virus, Hepatitis B Virus, and Hepatitis C Virus Transmission Through Organ Transplantation**

<table>
<thead>
<tr>
<th>Pre-transplant test</th>
<th>Timing of pre-transplant test</th>
<th>Posttransplant test</th>
<th>Timing of posttransplant test</th>
</tr>
</thead>
<tbody>
<tr>
<td>No recommendation on type of assay</td>
<td>During hospital admission for the organ transplant, but prior to organ implantation</td>
<td>HIV NAT or HIV Ag/Ab combination assay&lt;br&gt;HBV NAT&lt;br&gt;HCV NAT&lt;br&gt;HBV NAT and HBsAg&lt;br&gt;Anti-HBs, anti-HBc, and either HBV NAT or HBsAg</td>
<td>1–3 months&lt;br&gt;At 12 months</td>
</tr>
</tbody>
</table>

*Unless transplant patient infection was documented pre-transplant*

---

HIV: Human Immunodeficiency virus.  
HBV: Hepatitis B virus.  
NAT: Nucleic acid assay testing.  
HCV: Hepatitis C virus.  
Ag/Ab: Antigen and antibody.  

Public Health Reports: July-August 2013 Volume 128
Patient Safety Initiatives to Reduce Donor-derived Disease

Donor centers must report:

- "Relevant new post-transplant findings" to all accepting transplant centers including cultures, pathology findings, autopsy results
- Any “new disease or malignancy”… that may be transmitted to transplant recipients” to the Organ Procurement and Transplant Network (OPTN)

Donor and recipient centers must report:

- If concern for donor-derived disease arises to the OPTN patient safety system including:
  - Infection or disease in both donor and recipient
  - Similar disease in multiple recipients of same donor
  - Other substantive concern for donor origin of disease
Part of OPTN patient safety program

Examine and classify potential donor-derived transmission through transplantation of infection or malignancy

Educate transplant community

Help change policy and improve processes

Membership includes CDC, FDA, transplant centers, transplant infectious disease, lab testing, organ procurement organizations

<table>
<thead>
<tr>
<th></th>
<th>Deceased Donors N (%)</th>
<th>Living Donors N (%)</th>
<th>Total N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donors recovered</strong></td>
<td>40,223</td>
<td>31,278</td>
<td>71,501</td>
</tr>
<tr>
<td><strong>Donors with PDDTE</strong></td>
<td>763 (1.9%)</td>
<td>24 (0.08%)</td>
<td>787 (1.1%)</td>
</tr>
<tr>
<td><strong>Donors with proven/probable PDDTE</strong></td>
<td>141 (0.4%)</td>
<td>5 (0.02%)</td>
<td>146 (0.2%)</td>
</tr>
<tr>
<td><strong>Total recipient transplants performed</strong></td>
<td>110,402</td>
<td>31,277</td>
<td>141,679</td>
</tr>
<tr>
<td><strong>Recipients with proven/probable disease</strong></td>
<td>177 (0.16%)</td>
<td>4 (0.01%)</td>
<td>181 (0.13%)</td>
</tr>
<tr>
<td><strong>Recipient deaths due to proven/probable disease</strong></td>
<td>39 (0.04%)</td>
<td>1 (0.003%)</td>
<td>40 (0.03%)</td>
</tr>
</tbody>
</table>

33,407 individuals died between 2008-2012 while on the wait list

OPTN PDDTE: Potential donor-disease transmission events
Infection Reports to the DTAC: 2005-2011

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of Donor Reports</th>
<th>Number of Recipients with Confirmed Transmission</th>
<th>Number of DDD-Attributable Recipient Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus(^a)</td>
<td>166</td>
<td>48</td>
<td>16</td>
</tr>
<tr>
<td>Bacteria(^b)</td>
<td>118</td>
<td>34</td>
<td>9</td>
</tr>
<tr>
<td>Fungus(^c)</td>
<td>75</td>
<td>31</td>
<td>10</td>
</tr>
<tr>
<td>Mycobacteria(^d)</td>
<td>53</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Parasites(^e)</td>
<td>35</td>
<td>22</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total Infections</strong></td>
<td><strong>447</strong></td>
<td><strong>145</strong></td>
<td><strong>45</strong></td>
</tr>
</tbody>
</table>

In 2013: 31/284 (11%) cases reviewed by CDC

\(^a\) Adenovirus, HBV, HCV, HEV, HIV, HTLV, herpes simplex, influenza, LCMV, Parainfluenza (PIV)-3, Parvovirus B19, rabies, West Nile virus


\(^c\) Aspergillus spp, *Candida* spp, *Coccidioides imitis*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, zygomycetes

\(^d\) Tuberculosis, non-TB mycobacteria

\(^e\) Babesia, *Balmuthia mandrillaris*, Chagas (*Trypanosoma cruzi*), *Naegleria fowleri miasis*, *Strongyloides*

DTAC: Disease Transmission Advisory Committee  DDD: Donor-derived disease  Data includes cases classified as possible, probable or proven from 2005-2007 as published in AJT, and all reviewed cases from 2008-2011.
Variability of Reporting Suspected Donor-derived Diseases by Organ Procurement Organizations

Cases reported through 2013.
Selected DTAC Patient Safety Projects

- Demonstrated harm associated with universal HTLV-1/2 donor testing
- Formal guidance documents
  - TB risk assessment for living donors
  - Geographic and seasonally limited disease
  - West Nile virus testing
  - Central nervous system infections in deceased donors
  - Ebola virus disease screening for potential donors
- Translation of public health service guidelines for preventing transmission of HIV, HBV, HCV into policy
- Process to improve communication between organ procurement organizations and transplant centers

HTLV-1/2: Human T-cell lymphotropic virus, types 1 and 2
Novel Transplant-Associated Infections

Sherif R. Zaki, MD, PhD
Chief, Infectious Diseases Pathology Branch
Division of High-Consequence Pathogens and Pathology
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
Unexpected Donor-derived Infections Associated with Organ Transplantation

- Multiple challenges
  - Unexpected or unrecognized at time of death
  - Not screened for in donor
  - Unknown incidence (presumed low)
  - Associated with significant morbidity and mortality
  - High-profile events

Single donor → Multiple recipients
Unexpected Donor-derived Infections

Will Any Organ Do?

By Gretchen Reynolds

Doctors are confronting complex medical and ethical questions.

NY Times, 2005 (Rabies)

Officials Re-examining Organ Transplant Rules

Brain Infection in Two Patients Raises Issue

By Denise Grady

The plight of two kidney transplant patients who contracted a brain infection from an organ donor is prompting health officials to re-examine their policies on using people with certain neurovising in the patients' treatment.

NY Times, 2009 (Amoeba)

Transplant Patients Die of Rodent Disease

The Virus, Undetected in Organ Donors, Is Linked to 6 Cases

By Katie Zezima and Denise Grady

Three organ recipients in southern England have died in the past year of a disease that is seldom deadly for the rats and other small rodents from which the organ donors were infected.

NY Times, 2005 (LCMV)

West Nile Cases Raising Questions Over Transplants

No Test to Screen Blood Weeks Needed to Determine if Operation or a Transfusion Allowed Transmissions

NY Times, 2002 (WNV)
West Nile virus
- 6 clusters

Lymphocytic choriomeningitis virus
- 5 clusters

Rabies
- 2 clusters

Balamuthia
- 2 clusters

Microsporidiosis
- 2 clusters
West Nile Virus (WNV) in an Organ Donor and Four Transplant Recipients, August 2002

Organ DONOR
✓ Female victim of a car accident
✓ Received multiple transfusions
✓ Patient died

All organ RECIPIENTS became febrile (2 kidney, liver, heart)

One kidney recipient died
✓ Thought to have had WNV
✓ Seronegative for WNV

But IHC and PCR showed WNV encephalitis

Blood components from 63 donors
✓ Only one component was WNV IgM positive
✓ Only one component was WNV PCR positive, but WNV IgM negative

Stimulated trace back investigation

Viral antigens in red, IHC

IHC: Immunohistochemistry
PCR: Polymerase chain reaction
Organ DONOR:
✓ Male who died of a head trauma

All 4 organ RECEPIENTS died 9-76 days post-transplant

IHC confirmed LCMV in all recipients but lack of donor tissue tracing back to donor

Massive hepatocellular necrosis

Initial IHCs for herpesviruses and adenoviruses were negative

Viral antigens in red, IHC

LCMV culture results available after 6 weeks

LCMV: Lymphocytic choriomeningitis virus

Second LCMV Cluster in Three Transplant Recipients, 2005

Organ DONOR
✓ Woman who died of a stroke.

3 of 4 organ RECIPIENTS die 23-26 days post-transplant
1 renal recipient alive

Stimulated trace back investigations

Massive hepatocellular necrosis

IHC and PCR confirmed LCMV in tissues from all 4 recipients

Viral antigens in red, IHC
Where Did the Virus Come From?

- Donor’s daughter had a pet hamster that was sick
- Donor cleaned the cage and where the hamster played
Pet Rodents and Fatal Lymphocytic Choriomeningitis in Transplant Patients


As a Result, Risk Assessment and Screening Questions Improved

<table>
<thead>
<tr>
<th>Patient or Source of Specimen</th>
<th>Outcome or Status</th>
<th>Immunohistochemical Staining</th>
<th>Quantitative Real-Time RT-PCR†</th>
<th>Blood and Serum Testing</th>
<th>Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor</td>
<td>No reported disease</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Liver recipient†</td>
<td>Death 26 days after transplantation</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lung recipient¶</td>
<td>Death 23 days after transplantation</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Kidney Recipient B†</td>
<td>Death 23 days after transplantation</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Kidney Recipient A**</td>
<td>Survival</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hamster in donor’s household††</td>
<td>No reported disease</td>
<td>+</td>
<td>+</td>
<td>NT</td>
<td>–</td>
</tr>
<tr>
<td>Hamster’s caregiver¶¶</td>
<td>No reported symptoms</td>
<td>NA</td>
<td>–</td>
<td>+</td>
<td>–</td>
</tr>
</tbody>
</table>

*Table 2: Summary of Laboratory Evaluations for Lymphocytic Choriomeningitis Virus Infection in the 2005 Cluster.*
LCMV in a cluster of fatal transplant-associated disease

3 recipients from single donor who died with cerebral hemorrhage

100 times faster than Sanger sequencing

25 million bases in 4 hours

Viral antigens in red, IHC

A New Arenavirus in a Cluster of Fatal Transplant-Associated Diseases

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812
MARCH 6, 2008
VOL. 358 NO. 10

Third LCMV Cluster Detected Using Advanced Molecular Detection

LCMV: Lymphocytic choriomeningitis virus

Massively parallel sequencing

Yu-Hui Rogers and J. Craig Venter

A sequencing system has been developed that can read 25 million bases of genetic code — the entire genome of some fungi — within four hours. The
Another Unusual Infection Transmitted from Organ Donor to Four Transplant Recipients

- In 2004, CDC contacted by pathologist in Texas

- Two transplant recipients with unexplained deaths

- Third transplant recipient with altered mental status

- Connection of a common donor among cases was determined by families whose loved ones were in the intensive care unit

Twenty year-old Male Donor

Agitated, confused, delirious
Intubated in ER
Urine drug screen positive
Heart attack
Subarachnoid hemorrhage

Fallen 3 times
“Hyperventilating”
“He is very, very anxious”

Nausea/Vomiting
“I can’t even swallow my own spit”

Hospital C

Declaration of Death

Thought to have died from cocaine-induced brain hemorrhage. Organs transplanted.

Hospital B

Organ donor timeline, April–May 2004
Background on the Four Recipients at Hospital A, Texas

Organ recipient timeline, April–June 2004

Alabama: Lung recipient dies in OR

Liver

Kidney

Kidney

Home

Mild rejection

ICU

X

X

4-29 5-2 5-5 5-8 5-11 5-14 5-17 5-20 5-23 5-26 5-29 6-1 6-4 6-7 6-10 6-13 6-16 6-19 6-22
Negri bodies, indicating rabies!

Viral antigens in red, IHC

Histopathology & IHC, Rabies

Viral antigens in red, IHC
Recalled 4th death due to encephalitis in organ transplant recipient

Reviewed autopsy
- Consistent with viral encephalomyelitis due to West Nile virus
- Received liver transplant
- Different donor than other cases

Specimens sent to CDC for further investigation
Negri bodies again, indicating rabies!

Viral antigens in red, IHC
What Was the Source of Infection?

- Was there a link between first three cases and this case?
- Was the recipient’s infection unrelated to transplant?
- Was the second donor infected?
- Was this healthcare-worker transmitted rabies?
As a result, OPTN changed their requirements and instituted better tracking of donor organs and tissues.
Transmission of Rabies Virus from an Organ Donor to Four Transplant Recipients


Donor’s serum positive and sequence from all three recipients was exactly the same.
Kidney transplant recipient died 18 months post-transplant

Donor with a history of raccoon exposure died with fever, vomiting, seizures and dysphagia

Rabies positive by histopathology and PCR

Three other organ recipients completed post-exposure prophylaxis and remained asymptomatic with serum rabies neutralizing antibodies

IHC: Immunohistochemistry
PCR: Polymerase chain reaction
Impact from Clusters of Transmitted Rabies

- **From the bat cluster, we learned**
  - Rabies could be transmitted through solid organ transplant
  - Tracking the organs and tissues of each donor is critical

- **Instituted better mechanism to track donor and the multiple recipients**

- **From the raccoon cluster, we learned**
  - Rabies transmitted from raccoons may have a longer incubation
  - Three recipients were pre-emptively treated

- **Post-exposure prophylaxis was effective in recipients who received donor-infected organs, even for rabies**
An Unusual Infection in an Organ Donor and Four Transplant Recipients, 2009

Organ DONOR
✓ 4 year-old male
✓ Presumed to have died from ADEM following Influenza A infection
✓ Ring-enhancing brain lesions

3 organ RECEPIENTS
✓ 3 weeks after transplant, kidney recipient admitted with seizures and altered mental status
✓ Liver and heart recipients asymptomatic

From donor autopsy tissues, CDC found
✓ Granulomatous amebic encephalitis caused by Balamuthia mandrillaris

From further investigation
✓ Confirmed in both kidney recipients
✓ One kidney recipient died
✓ Other three recipients recovered with therapy

ADEM: Acute demyelinating encephalomyelitis
IHC: Immunohistochemistry
Another *Balamuthia* Infection Transmitted by Organ Donor to Four Transplant Recipients, 2010

- **Two of four transplant recipients present with encephalitis**
  - Common donor died from presumed stroke

- **Of the four transplant recipients**
  - Liver recipient already died
  - Kidney-pancreas recipient unconscious
  - Heart and other kidney recipients asymptomatic
Liver Recipient

- Post-transplant day (PTD) 18 presents with
  - Double vision and difficulty with walking
  - Febrile; loses consciousness
- Brain biopsy inconclusive
- Died on PTD 26

Neuroimaging: Ring-enhancing lesions

Liver at autopsy

Trophozoites
Kidney-Pancreas Recipient

Brain biopsy: IHC and PCR Balamuthia positive

Neuroimaging:
Ring-enhancing lesions

IHC: Immunohistochemistry
PCR: Polymerase chain reaction
Heart and other kidney recipients placed on pre-emptive antifungal therapy and survived
A Missed Connection in Donor

Neuroimaging:
Ring-enhancing lesion

Large skin lesion for 6-month duration
37 year-old Mexican woman living in El Paso
- Died of cerebrovascular accident (CVA) in September 2011

Left kidney and double lung recipients present with fever, tremors, neutropenia and encephalopathy

Right kidney recipient doing well

Outside tests show brucella IgM positive serologies

Left Kidney Recipient

- Left kidney recipient clinical condition deteriorates, necessitating nephrectomy

Micro-abscesses on surface of kidney
Microsporidia in Renal Tubules of Donor Left Kidney

Hematoxylin and eosin  Gram stain  Immunohistochemistry  Electron micrograph
Biopsy from Right Kidney Recipient

- All three recipients were infected by same genotype
- Right kidney recipient recovered after six months of albendazole therapy

Interstitial nephritis

IHC shows *Encephalitozoan* species

IHC: Immunohistochemistry
Unusual Transplant-associated Infections

- While unusual, they are more common than previously suspected
  - Once identified, the next one is easier to recognize
- Pathology plays a frontline role
  - Recognizing emerging infectious diseases
  - Guiding epidemiologic investigations
- Donor screening and autopsies are important
- Donor specimens should be stored
  - Allow future investigations after identification of novel infectious agents
Acknowledgements

- Division of High-Consequence Pathogens and Pathology
  - Infectious Diseases Pathology Branch
  - Viral Special Pathogens Branch
  - Poxvirus and Rabies Branch

- Division of Vector-Borne Diseases

- Division of Parasitic Diseases

- Division of Foodborne, Waterborne, and Environmental Diseases

- Division of Healthcare Quality Promotion

- Office of Blood, Organ, and Other Tissue Safety

- State Health Departments

- Academic Institutions
Since Mr. Sims is a vegetarian, I'll be submitting a request for an artichoke heart.
Preventing Unusual Transplant-associated Infections

Sridhar V. Basavaraju, MD

Medical Officer, Office of Blood, Organ, and Other Tissue Safety
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases
# Unusual Transplant-transmitted Infectious Encephalitis Clusters

Clusters in the United States, Reported to CDC, 2002-2014

<table>
<thead>
<tr>
<th>Infectious Agent</th>
<th>Total donors and clusters</th>
<th>Total Recipients</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Nile virus</td>
<td>6</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>LCMV</td>
<td>4</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Rabies</td>
<td>2</td>
<td>8</td>
<td>5*</td>
</tr>
<tr>
<td>Balamuthia mandrillaris</td>
<td>2</td>
<td>7</td>
<td>3**</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>14</strong></td>
<td><strong>44</strong></td>
<td><strong>22</strong></td>
</tr>
</tbody>
</table>

* Three recipients received rabies post-exposure prophylaxis and survived.
** Four recipients received prophylactic treatment.

LCMV: Lymphocytic choriomeningitis virus.
Common Themes in Unusual Transplant-transmitted Infection Clusters

- **Donor infection is unrecognized**
  - Diseases are rare and infrequently encountered
  - Some donors have no evidence of infectious cause of death
  - Other donors diagnosed with meningoencephalitis of unknown cause, but have evidence of infectious etiology including abnormal lumbar puncture

- **Disease risk factors are unknown** (e.g., microsporidia)

- **Donor risks and exposures are not clearly identified**
  - Next of kin complete the donor history questionnaire, but they may be unaware of exposures or certain behaviors
Common Themes in Unusual Transplant-transmitted Infection Clusters

- **Except for West Nile virus, donor screening tests are not available**

- **Difficulty in linking donor and recipient infections**
  - Difficult to recognize and diagnose in recipient
  - Geographic distance
  - Timeliness of information

- **Lack of active surveillance system**
Opportunities for Prevention
Passive versus Active Surveillance

- **Current reporting mechanism is passive**
  - Current passive reporting by transplant centers and OPO to OPTN/UNOS
  - Only report if concern for donor-derived infection arises

- **Establishment of active national surveillance system**
  - Routine reporting of total transplants performed
  - Implementation of case definition criteria
  - Electronic notification of all transplant centers if a case is suspected

OPO: Organ procurement organizations
OPTN: Organ Procurement and Transplantation Network
UNOS: United Network for Organ Sharing
Opportunities for Prevention
Better Screening of Donors

- Improve screening of donors
  - Standardized donor history questionnaire across all organ procurement organizations

- Balance need to identify donors with an increased risk of infectious encephalitis with the need to make the best use of every organ donated
Improving Recognition of Infectious Encephalitis in Donors

- Identifying donors with increased risk of infectious encephalitis through surveillance
  - Recognize signs and symptoms of infectious encephalitis
    - Use all information available (e.g., clinical data and donor history)
  - If increased risk is identified
    - Additional laboratory screening is triggered
    - Follow-up and monitor all recipients

- If infectious encephalitis is identified earlier, therapeutic or prophylactic intervention in recipients may save lives
Risk Stratification Model
Identifying Donors with Infectious Encephalitis

1. Clinical tool to identify donors with infectious encephalitis
   - Must distinguish infectious from non-infectious encephalitis
   - Use available clinical data including
     - Fever and other symptoms
     - Cerebrospinal fluid analysis
     - Imaging results (e.g., CT, MRI and x-rays)
   - Incorporate donor history questionnaire
Risk Stratification Model
Optimizing Organ Allocation

2. Properly allocate organs from donors with infectious encephalitis
   - Maximize survival benefit for recipients

3. Re-optimize organ allocation algorithm
   - Reduce the overall “opportunity cost” on the organ match system
   - Ensure the best fit for an organ identified as at increased risk
Risk Stratification Model
Steps to Implementation

- CDC clinicians and epidemiologists identify clinically relevant variables from infectious and non-infectious case reports

- OPTN/UNOS provides data on patient characteristics for those waiting for organs

- Data analyzed by a team in ISyE at Georgia Tech using process optimization techniques aimed at solving efficiency problems

OPTN: Organ Procurement and Transplantation Network
UNOS: United Network for Organ Sharing
ISyE: Industrial and Systems Engineering Department
Improving the Safety of Organ Transplantation

- Risk for these unusual donor-derived infections is low
- Benefits of organ transplant far outweigh the risks
- Risk assessment should use relevant data to inform decision-making
- CDC and organ transplant community continue to collaborate to reduce the risk of transplant-transmitted infections
Organ donors save more than 75 lives every day.
Register as an organ, eye, and tissue donor.