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

Daniel Kaul MD
Associate Professor
University of Michigan

CEOT
CUTTING EDGE OF TRANSPLANTATION

AST | AMERICAN SOCIETY OF TRANSPLANTATION

RESOLVING THE ORGAN SHORTAGE

PRACTICE | POLICY | POLITICS

FEBRUARY 25-27, 2016 • PHOENIX, ARIZONA

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

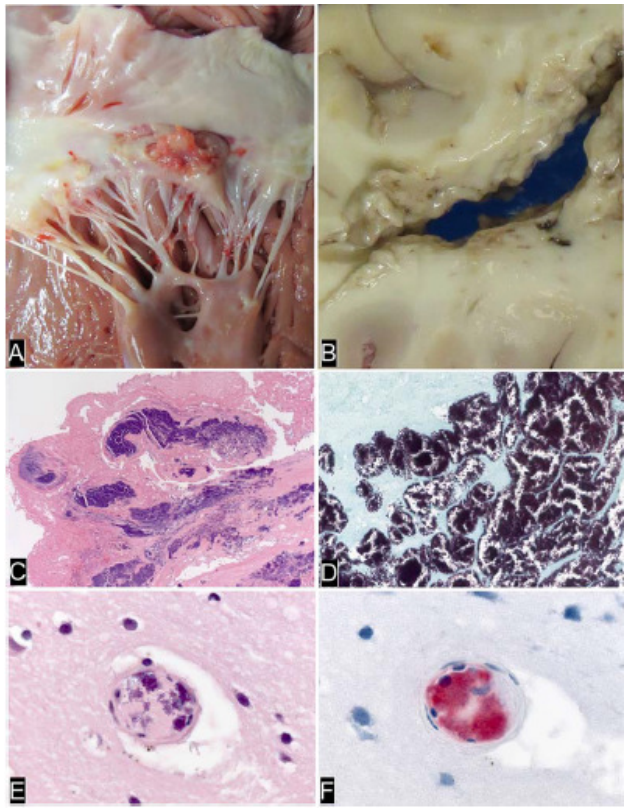
- **Site specific protocols are used**
- **West Nile virus nucleic acid amplification testing**
  - During periods of increased mosquito activity or known outbreaks
- ***Trypansoma cruzi* (serology)**
  - At-risk donors
- **Coccidiomycosis (serology)**
  - Southwestern states
- **Strongyloides (serology)**
- **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

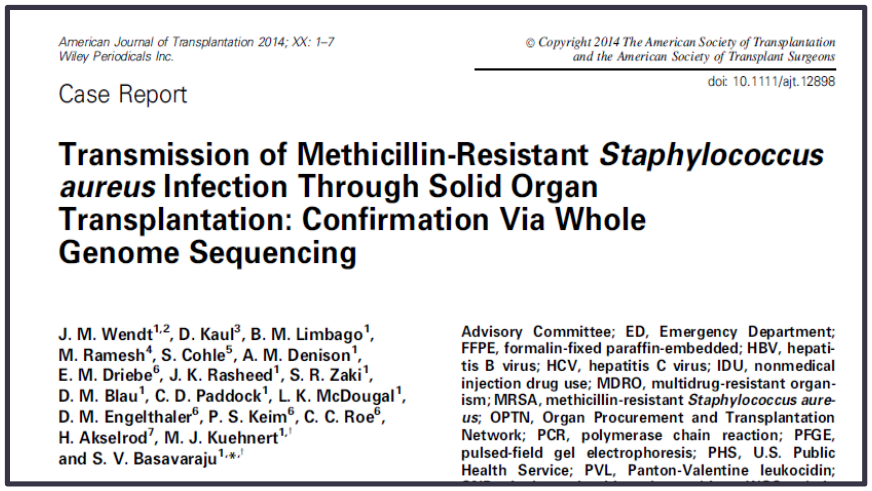
- **Potential donor: male with injection drug use**
  - MRSA bacteremia
  - Septic emboli to brain
  - Afebrile, on antibiotics for more than 48 hours
- **Recipient critically ill**
  - End stage pulmonary fibrosis
  - Mechanical ventilation in ICU
- **Should organs from this donor be transplanted?**



MRSA: Methicillin-resistant Staphylococcus aureus
ICU: Intensive care unit.
Wendt JM, et al. *Am J Transplant*, 2014

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



American Journal of Transplantation 2014; XX: 1–7
Wiley Periodicals Inc.

doi: 10.1111/ajt.12898

Case Report

Transmission of Methicillin-Resistant *Staphylococcus aureus* Infection Through Solid Organ Transplantation: Confirmation Via Whole Genome Sequencing

J. M. Wendt[1,2], D. Kaul[3], B. M. Limbago[1], M. Ramesh[4], S. Cohle[5], A. M. Denison[1], E. M. Driebe[6], J. K. Rasheed[1], S. R. Zaki[1], D. M. Blau[1], C. D. Paddock[1], L. K. McDougal[1], D. M. Engelthaler[6], P. S. Keim[6], C. C. Roe[6], H. Akselrod[7], M. J. Kuehnert[1,†] and S. V. Basavaraju[1,*,†]

Advisory Committee; ED, Emergency Department; FFPE, formalin-fixed paraffin-embedded; HBV, hepatitis B virus; HCV, hepatitis C virus; IDU, nonmedical injection drug use; MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; OPTN, Organ Procurement and Transplantation Network; PCR, polymerase chain reaction; PFGE, pulsed-field gel electrophoresis; PHS, U.S. Public Health Service; PVL, Panton-Valentine leukocidin;

- Both infected recipients doing well > one year after transplant

Donors with bacteremia or endocarditis

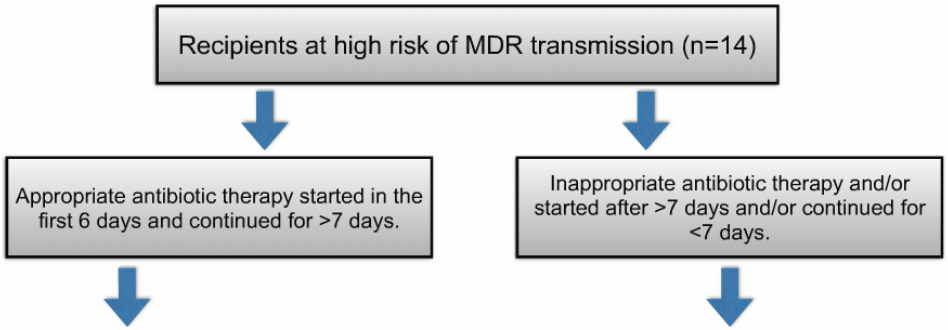
- About 5% of donors have bacteremia at procurement
- Outcomes good
  - Recipient and donor treated
  - Not an MDR organism
  - Typically treat recipients for 7 days
- Donors with endocarditis
  - One publication with 5 donors with good outcomes
  - 4/5 with coagulase negative staph, one with enterococcus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

American Journal of Transplantation 2005; 5: 781–787

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

SOT Using Donors With MDR Bacteria



Recipient	Pathogen	Transmission
1A	CRKP	NO
2A	CRKP	NO
3A	CRAB	NO
3B	CRAB	NO
4A	CRAB	NO
8A	CRAB	NO
9A	CRAB	NO
10A	CRAB/CRKP	NO

Recipient	Pathogen	Event	Reason	Transmission	Outcome
1B	CRKP	Inappropriate therapy	Risk underestimated	YES	Infection
1C	CRKP	Inappropriate therapy	Risk underestimated	YES	Colonization
2B	CRKP	Insufficient duration	Miscommunication	YES	Infection
5A	CRAB	Inappropriate therapy	Miscommunication	NO	N/A
6A	CRKP	Started >7 days	Miscommunication	YES	Infection
7A	CRAB	Started >7 days	Risk underestimated	NO	N/A

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, blood stream infection.

American Journal of Transplantation 2015; 15: 2674–2682

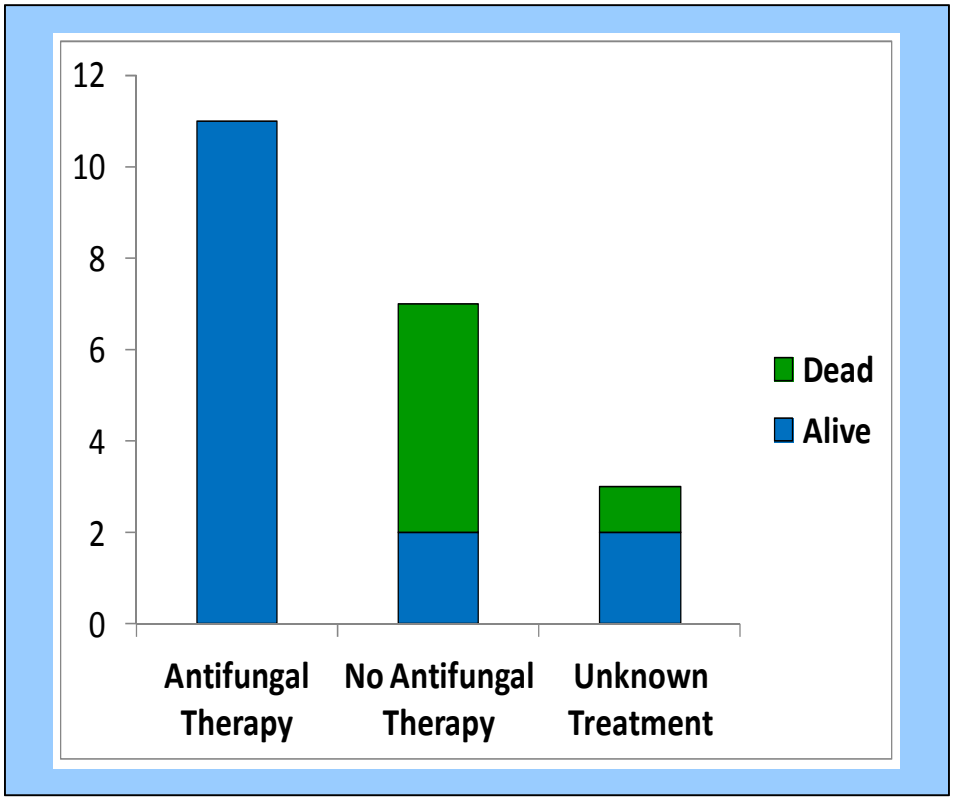
Endemic infections may present later after transplant

	0-30 days	31-90 days	91-180 days	> 180 days
Viral	LCM WNV (4) RSV	CMV (3) Parvovirus WNV	Hepatitis C	Hepatitis B
Bacterial	Assorted (23)	Klebseilla		
Fungal	Candida (3) Coccidioides (6) Aspergillus Cryptococcus (4) Scopulariopsis Zygomycete (2)	Aspergillus Coccidioides (3) Histoplasmosis		Aspergillus
Mycobacterial	M. tuberculosis (2)	M. tuberculosis (2)	M. tuberculosis (2)	
Parasitic	Toxoplasma Balamuthia (5)	Strongyloides Toxoplasma Encephalitozoon (2)	Strongyloides (2) Toxoplasma Encephalitozoon Balamuthia	

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

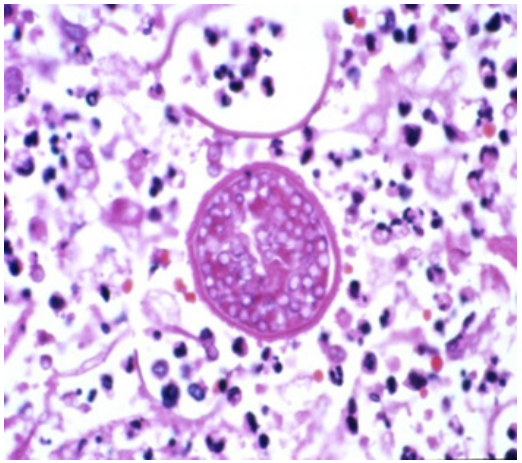
Dx median 30 days

6 deaths median 21 days post tx

Kusne[1], S Taranto[2], S Covington[2], D Kaul[1], W Bell[1], SW Biggins[1], E Blumberg[1], GD DeStefano[1], E Dominguez[1], D Ennis[1], M Klassen-Fischer[1], C Kotton[1], Y Law[1] , M Menegus[1], R Miller[1], M Pavlakis[1], TL Pruett[1], D LaPointe Rudow[1], P Ruiz[1], N Siparsky[1], M Souter[1], L Weiss[1], C Wolfe[1], and M Green[1]. [1]OPTN Ad Hoc Diseases Transmission Advisory Committee. [2]United Network or Organ Sharing ATC 2013 Seattle

Coccidomycosis

- 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)



American Journal of Transplantation 2012; 12: 2414–2428

http://optn.transplant.hrsa.gov/media/1138/seasonal_disease_guidance.pdf

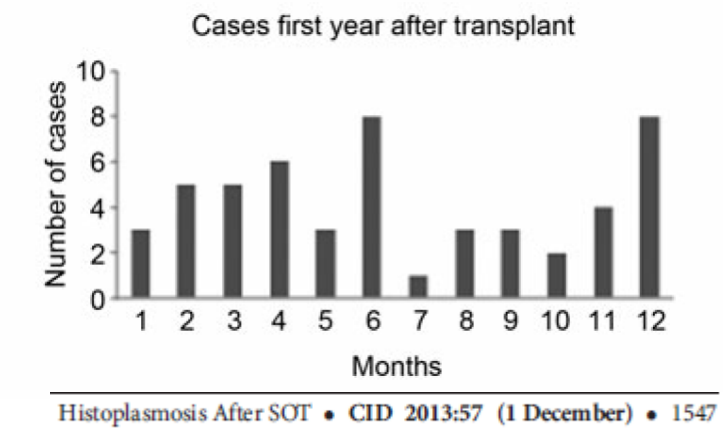
Blair JE, Mulligan DC. Coccidioidomycosis in healthy persons evaluated for liver or kidney donation. Transpl Infect Dis 2007

Donor-derived Histoplasmosis

Histoplasmosis After Solid Organ Transplant

Maha Assi,[1] Stanley Martin,[2] L. Joseph Wheat,[3] Chadi Hage,[4] Alison Freifeld,[5] Robin Avery,[6] John W. Baddley,[7] Paschalis Vergidis,[8] Rachel Miller,[9] David Andes,[10] Jo-Anne H. Young,[11] Kassem Hammoud,[12] Shirish Huprikar,[13] David McKinsey,[14] Thein Myint,[15] Julia Garcia-Diaz,[16] Eden Esguerra,[17] E. J. Kwak,[18] Michele Morris,[19] Kathleen M. Mullane,[20] Vidhya Prakash,[21] Steven D. Burdette,[22] Mohammad Sandid,[1] Jana Dickter,[23] Darin Ostrander,[24] Smyrna Abou Antoun,[1] and Daniel R. Kaul[25]

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



Brief Report

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. COOKSON, 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

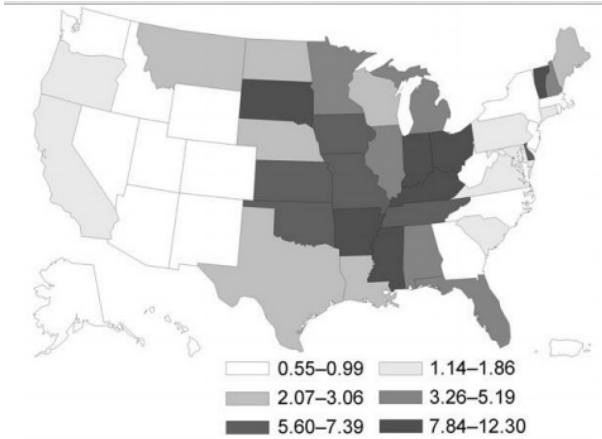
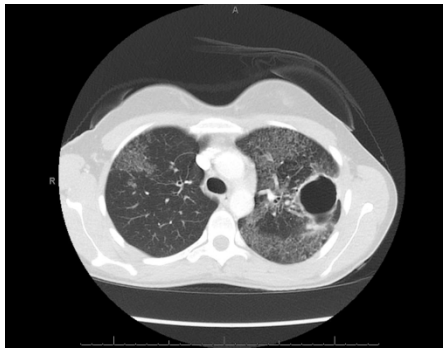


Figure 1. Geographic distribution of histoplasmosis in persons ≥65 years of age, United States, 1999–2008. Values are no. cases/100,000 person-years.
Downloaded from http://wwwnc.cdc.gov/eid/article/17/9/10-1987-f1.htm *on July 8, 2014.*

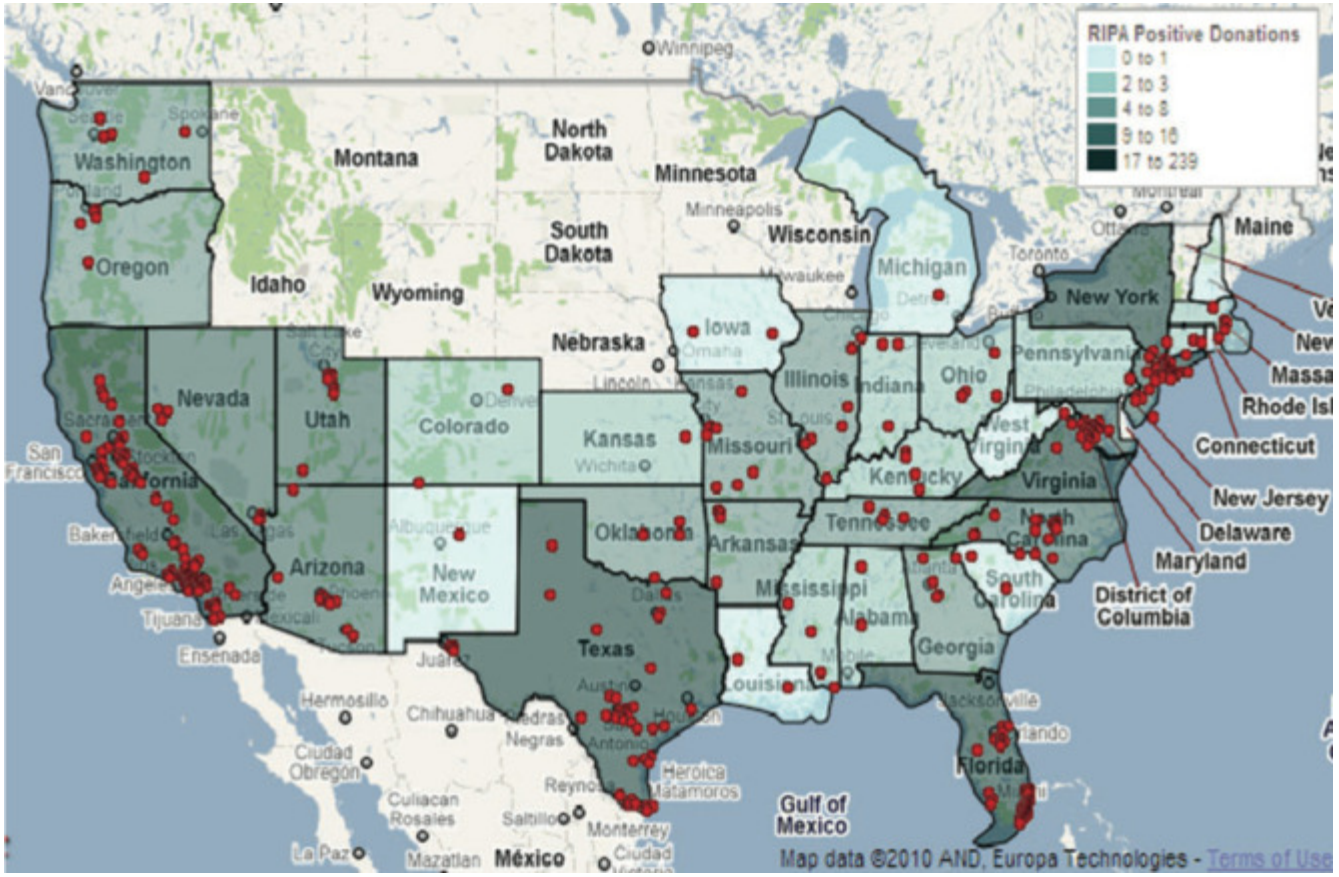


http://optn.transplant.hrsa.gov/media/1138/seasonal_disease_guidance.pdf

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)

Strongyloides

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

Investigation	Year	State	Age/Sex	Birth country	Duration of US residence (years)	Cause of death
1	2009	NY	55/M	West Indies	21	Head trauma in motor vehicle accident (MVA)
2	2009	NV	58/F	Honduras	Unknown	Respiratory failure due to asthma exacerbation
3[#2]	2010	PA	54/M	Dominican Republic	2.5	Head trauma secondary to gunshot wound (GSW)
4[#20]	2011	MA	46/M	Honduras	7	Trauma in MVA
5[†]	2012	NY	45/M	Guyana	14	Cardiac arrest, subarachnoid hemorrhage
6[†]	2012	FL	49/M	United States	Unknown	Subdural hematoma
7[#6,10]	2012	PA	24/M	Puerto Rico	8	Head trauma secondary to GSW

- 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.

American Journal of Transplantation 2015; 15: 1369–1375
Wiley Periodicals Inc.

Donor-derived West Nile Virus

TABLE 2. Characteristics of published organ donors transmitting WNV infection

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

[a] Tested negative by NAT, nucleic acid amplification.
[b] No. of donors positive/No. of donors tested.
WNV, West Nile virus; PCR, polymerase chain reaction.

RECIPIENT DISEASE

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

Transplantation • Volume 97, Number 9, May 15, 2014

WNV screening tests

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

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

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

http://optn.transplant.hrsa.gov/sharedcontentdocuments/west_nile_virus_living_donors.pdf

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

https://www.transplantpro.org/news/guidance-for-organ-donation-and-transplantation-professionals-regarding-the-zika-virus/

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