Objectives

• To understand common contemporary scenarios in donor derived infections that may affect screening decisions

• To know how the recent CDC/PHS guidelines may impact safety of organ donation

• To elaborate what perioperative transplant professionals can do to mitigate the risk of disease transmission
Disclosures

None
Infection in Transplantation

• 25% of cadaver kidneys have bacterial contamination at time of transplant
• Occurs in 70% of patients in the first year
• Remains a leading cause of death
• Risks
  – Epidemiologic exposure and history
  – Net state of immunosuppression
  – Time after transplant
  – Efficacy of prophylaxis
Case 1

• Transplant recipient identified with post-transplant HCV and HIV infection with no obvious risk factors. Negative pre-transplant testing

• Reported to OPO, UNOS, and CDC

• Donor – Look-back Assessment
  – Negative serology for HIV & HCV
  – Appropriately labeled as “high risk” by PHS Guidelines
  – Subsequent testing of post-transfusion serum was + for HIV and HCV by PCR

• All other recipients tested + for HIV & HCV

Case 1: Something to fear?

The ugly

• Transplant recipient identified with post-transplant HCV and HIV infection with no obvious risk factors. Negative pre-transplant testing

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4 cases of HIV transmitted since HIV antibody testing

• All occurred when testing consisted of HIV Ab NOT molecular (NAT) testing

• Factors that may lead to HIV transmission
  – Hemodilution
  – Living donor tested, then converts after testing and before donation
  – HIV Ab test negative (window period) before seroconversion
Limitations of organ donor screening

- Restricted timeline
- Different screening paradigms
- Donor history
- Incomplete data collection
- Serology-based screening
- Variable NAT capacity and practice
- No expectation for “Zero Risk”

Ison & Nalesnik. Am J Transplant. 2011; 11
Definition
CDC high risk

• **1994**: CDC published guidelines for preventing HIV transmission through Organ Transplant

• ‘Further recommendations should be made to reduce the already LOW RISK of HIV transmission by transplantation’

• **2013**: Revised guidelines

Seem et al, Public Health Reports. 2013; 128
Definition
CDC high risk (revised 2013)

- **Men who have sex with men** (MSM) – men who have had sex with another man in the preceding 5 years–12 months
- **Hemophiliac** – persons with hemophilia who have received human derived clotting factor concentrates
- **Injection drug use** – nonmedical IV/IM/SC injection of drugs in the preceding 5 years–12 months
- **Commercial sex worker** – persons having sex in exchange for money or drugs in preceding 5 years–12 months
- **High risk sex** – exposed in preceding 12 months to known/suspected HIV infected blood or persons in above four categories
- **New STD** – syphilis, gonorrhea, chlamydia, genital ulcers in preceding 12 months
- **Incarcerated** – Inmate of correctional system for at least 72 hours and in the past year
- **Hemodialysis** last 12 months (for HCV)

Seem et al, Public Health Reports. 2013; 128
Window period

• Between acquisition of infection, and serologic detectability:
  – HIV: 22 days
  – HCV: 66 days

• With NAT (molecular) testing:
  – HIV: 9 days (8-10)
  – HCV: 7 days
Window period

HIV risk

• HIV ELISA: 0.09 – 12.1 per 10,000

• HIV NAT (molecular): 0.04 – 4.9 per 10,000
  – Injection drug users: 4.9
  – Men who have sex with men: 4.2
  – Commercial sex workers: 2.7
  – Incarcerated: 0.9
  – Blood exposure: 0.6
  – High risk sex: 0.3
  – Hemophiliacs: 0.035
Window period

HCV risk

• HCV ELISA: 0.26 – 300.6 per 10,000

• HCV NAT (molecular): 0.027 – 32.4 per 10,000
  – Injection drug users: 32.4
  – Men who have sex with men: 3.5
  – Commercial sex workers: 12.3
  – Incarcerated: 0.8
  – Blood exposure: 0.4
  – Hemophiliacs: 0.027
Patient attitudes

Turn down high risk donors

- In focus groups, patients felt unprepared to receive organ offers, especially from high risk donors (HRD)
- They want information about HRD behaviors, kidney quality and probability of undetected infection
- Patients weighed opinion of their nephrologist most heavily when deciding about organ offers
- Conclusion: Lack of preparedness contributes to patient apprehension toward HRD organs
- Need for ongoing education
  - Patients
  - REFERRING NEPHROLOGISTS – the most trusted source of information

Clin Transplant 2012 Ros et al (Johns Hopkins)
## What is high risk?

### Odds of... 

<table>
<thead>
<tr>
<th>Event</th>
<th>Per 10,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Being struck by lightening in your lifetime (80 years)</td>
<td>1</td>
</tr>
<tr>
<td>Dying in a plane crash in your lifetime</td>
<td>2</td>
</tr>
<tr>
<td>Dying in a car accident</td>
<td>125</td>
</tr>
<tr>
<td>Dying crossing the street</td>
<td>16</td>
</tr>
<tr>
<td>Missing HIV with a NAT test</td>
<td>0.04 – 5</td>
</tr>
<tr>
<td>Missing HCV with a NAT test</td>
<td>0.03 – 32</td>
</tr>
<tr>
<td>Dying if no liver transplant and MELD 20-29 in next 3 months</td>
<td>2,000</td>
</tr>
<tr>
<td>Dying if on waitlist and no kidney transplant in 1 year</td>
<td>900</td>
</tr>
</tbody>
</table>
Most recent case of HIV transmission was in a living donor

- Living donor had history of syphilis, and history of sex with male partners
- Initial evaluation and serologic tests were negative 10 weeks before donation
- Donation and transplant occurred, febrile illness in recipient, HIV positive test in recipient and donor – genetically identical strains
- After transmission documented, living donor reported unprotected sex with one man during year before donation (including interval between testing and donation) with unknown HIV status
Case 2

- Patient is a 46 year-old Chinese male
- Underwent cadaveric renal transplant
- CMV D+/R–
- Prophylaxis: Valganciclovir
- 9 days post-transplant
- Donor has + blood cultures drawn the day prior to donation
- Positive for Pseudomonas aeruginosa
Case 2

The good

- Patient is a 46 year-old Chinese male
- Underwent cadaveric renal transplant
- CMV D+/R–
- Prophylaxis: Valganciclovir
- 9 days post-transplant
- Donor has + blood cultures drawn the day prior to donation
- Positive for Pseudomonas aeruginosa
• Positive result on cultures
• Day of transplant
• Took several days to convey results to recipient centers
• Patient was receiving ciprofloxacin for a probable UTI, which covered the bacteria with no serious sequelae
Case 3

- Patient is a 56 year-old Chinese female with cirrhosis from chronic hepatitis B
- On liver transplant waiting list
- PPD 10mm
- Had BCG as a child
- AST 50, ALT 200, Tbili 2.0, MELD 30
- What do you do?
Case 3
The good

- Patient is a 56 year-old Chinese female with cirrhosis from chronic hepatitis B
- On liver transplant waiting list
- PPD 10mm
- Had BCG as a child
- AST 50, ALT 200, Tbili 2.0, MELD 30
- What do you do?
Recipient Evaluation / Diagnosis

- 2-step TST (≥5mm is positive) or IGRA; likely disregard prior BCG status
- CXR
- Careful history: risk factors, travel / residence to endemic countries, contact to active TB case, past prior rx/dx
- Symptom review
- If evidence for “old” granulomatous disease, e.g. apical thickening/scarring/nodularity:
  - Obtain sputa for AFB
  - If sputa neg / CXR stable, then expedite treatment
  - Even if TST / IGRA neg, would consider LTBI treatment, esp if TB risk factors present

Donor Evaluation / Diagnosis

• Living
  – Careful history: risk factors, travel / residence to endemic countries, contact to active TB case, past prior rx/dx
  – Symptom review
  – TST or IGRA

• Deceased
  – Careful history from family if possible, as above
  – IGRA
  – CXR
  – Cultures (if above abnl)

LTBI treatment options

- Isoniazid (INH)

Alternatives (with less data):
- Rifampin (RIF)
- Isoniazid-Rifapentine (3HP)
- Fluoroquinolone +/- ethambutol (MDR)

LTBI treatment is varied

INH

- Preferred treatment for LTBI → 9 months
- Concern for risk of hepatotoxicity, however, studies suggest low risk in compensated cirrhosis.

INH safety / efficacy

• Meta-analysis: 7 studies (2 prospective, 5 retro)
• 224 patients with positive pre-transplant TST
  – ≥6 mo INH: 61 (no development of active TB)
  – <6 mo INH: 16
  – RIF: 5
  – No rx: 143 (5.1% developed active MTB)
• INH ≥6 mo associated with decreased risk of active TB (8.2% absolute RR, p=0.02)
• 6% pts d/c’d INH due to hepatotoxicity; 1 pt with drug-induced liver failure
INH + Rifapentine (3HP)

- Recommended as an equal alternative to INH x 9 mo in healthy patients ≥12 yo and HIV-infected patients not on ART.

- Not recommended in the following:
  - Children <2yo
  - HIV-infected patients on any ART
  - Pregnant or planning to become pregnant
  - Contact to INH/RIF resistant cases
  - No / limited data on transplant / immunocompromised

Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection. MMWR 2011;60:1650–1653
# Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection

<table>
<thead>
<tr>
<th></th>
<th>INH-RPT</th>
<th>INH</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>3,986</td>
<td>3,745</td>
</tr>
<tr>
<td>Administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Directly-observed</td>
<td></td>
<td>Self-administered</td>
</tr>
<tr>
<td>therapy</td>
<td></td>
<td>therapy</td>
</tr>
<tr>
<td>Frequency</td>
<td>Weekly</td>
<td>Daily</td>
</tr>
<tr>
<td>Duration</td>
<td>12 weeks</td>
<td>9 months</td>
</tr>
</tbody>
</table>

Pre-transplant evaluation

- HIV
- HBV: HBsAg, HBSAb, HBcAb
- HCV
- Herpesvirus: HSV, VZV, CMV, EBV
- Syphilis
- Toxoplasma gondii (heart)

- Urinalysis
- Urine culture
- TST or IGRA
- CXR
- Sputum or BAL (lung)

- Blood cultures (depends)
- Others (next talk)
HIV positive recipient evaluation

<table>
<thead>
<tr>
<th>Eligibility criteria for HIV-infected transplant candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Meet center-specific criteria for specific organ transplant</strong></td>
</tr>
<tr>
<td>HIV-related criteria</td>
</tr>
<tr>
<td>Kidney: CD4+ T-cell count greater than 200 cells/μL</td>
</tr>
<tr>
<td>Liver: CD4+ T-cell count greater than 100 cells/μL (CD4+ T-cell count &gt;200 cells/μL if history of opportunistic infection or malignancy)</td>
</tr>
<tr>
<td>HIV RNA suppressed for kidney transplant recipients</td>
</tr>
<tr>
<td>HIV RNA suppressed for liver transplant recipients, or expected to be suppressed if unable to tolerate cART</td>
</tr>
<tr>
<td>Stable antiretroviral regimen</td>
</tr>
<tr>
<td>No active opportunistic infection or neoplasm</td>
</tr>
<tr>
<td>No history of chronic cryptosporidiosis, primary central nervous system lymphoma or progressive multifocal leukoencephalopathy</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Liver (HCV): BMI greater than 21 kg/m², no need for combined kidney transplant, no HCV+ donor</td>
</tr>
</tbody>
</table>

Chin-Hong PV et al, Infect Dis Clinics NA, 2013
# HIV to HIV transplant in South Africa

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>47</td>
<td>56</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>Sex</td>
<td>male</td>
<td>male</td>
<td>male</td>
<td>female</td>
</tr>
<tr>
<td>CD4 count (baseline)</td>
<td>288</td>
<td>258</td>
<td>132</td>
<td>147</td>
</tr>
<tr>
<td>CD4 count (12 mo)</td>
<td>253</td>
<td>119</td>
<td>112</td>
<td>220</td>
</tr>
<tr>
<td>HIV viral load (12 mo)</td>
<td>&lt;50</td>
<td>&lt;50</td>
<td>&lt;50</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>tacrolimus</td>
<td>tacrolimus</td>
<td>tacrolimus</td>
<td>tacrolimus</td>
</tr>
<tr>
<td>Clinical status</td>
<td>alive with functioning graft</td>
<td>alive with functioning graft</td>
<td>alive with functioning graft</td>
<td>alive with functioning graft</td>
</tr>
</tbody>
</table>

Muller E et al, NEJM; 2010; 362
HIV to HIV transplant in South Africa

Patient survival

1 Year patient survival 86.36%; 3 year patient survival 72.73%

courtesy E Muller
Obama lifts ban on HIV organ transplants
SF Gate
November 21, 2013

HIV-positive organ donation: HOPE Act signed into law
Slate
November 22, 2013
What happened

• 1988: Amendment to the National Organ Transplant Act of 1984 banned the transplant of any organ from a person with HIV
• February 14, 2013: Bipartisan Hope Act introduced in both houses of Congress
• Drafted by Rep. Lois Capps (D-CA) [RN], Senators Barbara Boxer (D-CA) and Tom Coburn (R-OK) [MD]
• Potential for almost **500** people on the donor list to receive organs from HIV-infected donors every year
• November 21, 2013: President Obama signs S.330: the HIV Organ Policy Equity Act
What transplant professionals can do peri-operatively

- Ensure **donor screening** performed
  - Review medical & social history
  - Physical examination
  - Screening of blood samples of donor and recipient
  - Serology
  - Nucleic Acid Testing (NAT)
  - LTBI assessment

- Define the **increased risk** donor
  - OPTN-defined increased risk donor
  - New definitions
  - Increased risk of transmission of other infections may affect peri-transplant antimicrobials

- Screen high-risk recipients **post-transplant**
Screening 123

1. The "**Big 3**": HIV, Hep B, Hep C
2. The **givens**: CMV, EBV, HSV, VZV, toxoplasma, syphilis, bacteria

*To be continued...*

Hocevar S et al, Ann Intern Med; 2014; 160(4)
Kotton C, Ann Intern Med; 2014; 160(4)
Objectives

• To understand common contemporary scenarios in donor derived infections that may affect screening decisions
• To know how the recent CDC/PHS guidelines may impact safety of organ donation
• To elaborate what perioperative transplant professionals can do to mitigate the risk of disease transmission