Achieving Consensus on Increased Risk Donors to Improve Access to Organ Transplantation

Executive Summary

Introduction
To address the current shortage of organs for transplantation, (114,651 candidates listed as of 6/8/12 while 28,538 transplants were performed in 2011) there has been increased use of donors at increased risk for transmission of infectious diseases. Recent transmission events involving both live and deceased donors has drawn attention to this pool of donors. As a result, OPTN policy was drafted, utilizing the exclusionary criteria from the 1994 “Guidelines for Preventing Transmission of Human Immunodeficiency Virus through Transplantation of Human Tissue and Organs,” to define donors at increased risk of infectious disease transmission (previously referred to as “high risk donors”). Although these guidelines are currently being revised by the US Public Health Service (PHS), there has been controversy about which donors warrant labeling as increased risk since doing so may result in reduced utilization of organs from increased risk donors. OPTN policy and CMS guidelines also requires special informed consent from candidates before transplantation utilizing organs from such increased risk donors, although specifics about how to conduct such consents has not been defined. Lastly, guidelines have been developed by the USPHS with regard to screening of live donors and for testing of recipients of organs from increased risk donors, but implementation in the transplant community has been variable. Despite the establishment of policy and guidelines about defining and screening donors at increased risk of infectious diseases transmission and the consenting and subsequent testing of recipients of organs from these donors, the evidence supporting practice has not been extensively reviewed.

Methods
We were funded by the Agency for Healthcare Research and Quality (AHRQ 1R13HS021060-01) to conduct a consensus conference of the transplant community to review the existing evidence:

1. To develop a consensus definition of donors at increased risk of transmission of HIV, HBV, and HCV
2. To define the optimal evaluation of living donors to mitigate against infectious disease transmission, with a focus on HIV, HBV, and HCV
3. To define the optimal timing, content, and method of informed consent of candidates considering accepting an organ from an increased risk donor
4. To develop consensus on the optimal evaluation of recipients of organs from an increased risk donors

Further, the meeting identified gaps in current knowledge on these issues that, in the opinion of the transplant community, need to be research to inform future policy and practice.

Individual with a diverse range of expertise, including physicians, surgeons, ethicists, patients and donor advocates, were invited to participate in the 4 working groups (see acknowledgements). Each group conducted a literature search to review available evidence to support recommendations and identify gaps in knowledge for their topic. These were discussed during a series of conference calls leading up to presentation of the working groups formal findings and recommendations at an in-person meeting held in Chicago, Illinois on April 27, 2012. During the in-person meeting, there was ample time to allow attendees to ask questions
and discuss the recommendations and findings of the working groups. Members of the working groups in attendance then voted to approve formal recommendations.

**Establishing a Consensus Definition of Donors at Increased Risk of Transmission of HIV, HBV, and HCV**

*Key Findings and Recommendations*

The working group reviewed the risk factors that are proposed for the revised PHS and developed consensus on how accurately the factor could be identified through donor histories, the strength of data to suggest that the factor is a risk for recent infection and on what proportion the donor population would be classified by the specific risk factor. It was opined that optimally risk factors that occur in less than 10% of the donor population, that represent a significant (>1:10,000 donors) and can be assessed reliably should be included in a definition for increased risk donors.

**Identified Gaps in Knowledge**

There were significant gaps in knowledge required to optimally define donors at increased risk of HIV, HBV or HCV transmission. Specifically, there was limited data on actual residual risk of HIV, HBV and HCV drawn from organ donors. Current data is not collected with sufficient detail about individual risk factors and studies of patient attitudes, concerns, and priorities regarding infectious risk and the specific categories used to define increased infectious risk have not been undertaken.

**Defining the Optimal Evaluation of Living Donors to Mitigate Against Transmission of HIV, HBV, and HCV**

*Key Findings and Recommendations*

The work group recommended that all live donors should be screened for risk behaviors for HIV, HBV and HCV and be educated on how to avoid contracting these infections during the period of time prior to organ procurement. Likewise, all live donors should have serology for HIV, HBV and HCV assessed at any time point in the donor evaluation process; such testing would identify donors with prior infection. Donors with positive test results should be referred for care of the underlying condition and recipients should be told that the donor is not medically suitable if the center decides not to proceed with using an organ from the infected donor. All live donors, irrespective of risk status, should be screened within 30 days but preferably within 14 days prior to surgery by HIV NAT, HBsAg, and HCV NAT to detect acute infection prior to donation.

**Identified Gaps in Knowledge**

There are a large number of gaps in our understanding of live donor screening. There is limited data on the cost of implementation of the various testing strategies. Likewise, there is limited data on the yield of live donor screening in additional to the incidence and risk factors for false positive results of testing living donors. The psychological impact on the potential donor of false positive results has not been analyzed to date either. Lastly, since FDA-approved, licensed or cleared screening assays may not be available at all live donor transplant centers, the test characteristics and yield, including false positive and negative results, of FDA-approved and “home brew” assays for quantitative and qualitative PCR for HIV, HBV and HCV when utilized for live donor screening are not well characterized. A funded prospective study of all or select centers to look at the testing characteristics and results would inform the development of evidence-based policy.
Defining the Optimal Timing, Content, and Methods of Informed Consent of Candidates Considering Accepting an Organ from a Donor at Increased Risk of HIV, HBV, and HCV Transmission

Key Findings and Recommendations
The work group agreed that, in general, live donors should be to allow disclosure of their relevant medical and social information to the potential recipient; without this, it is impossible to discuss specific risks posed to the recipient. The consent process should, in general, be the same when a candidate is considering organs from an increased risk live or deceased organ donor. Education about increased risk donors should be provided at the time of listing for organ transplantation and again at the time of the organ offer. This education should be reinforced during the waiting period between listing and organ offer, particularly if wait times are long. The consent should be obtained by a knowledgeable, trained clinician who can answer specific questions about the risks posed. The discussion of risk should be described as a continuum with the donor issues placed in context of all risks associated with transplantation. The consent should be individualized to the specific donor-recipient pair and information should be provided in a comprehensible way, allowing the recipient to engage their social support (family, friends, and others) during the consent process. Finally, the consent process must be clearly documented in the medical record.

Identified Gaps in Knowledge
Few studies are available to inform the optimal timing, content, and method of disclosing information and obtaining informed consent of candidates considering accepting organs from donors with identified risk factors for HIV, HBV, and HCV. Although it is possible to extrapolate from studies of consent in other clinical situations, further research is needed to inform the optimization of the consent process of organ transplant candidates. Specifically, little is known as to whether providing special informed consent by candidates accepting organs from increased risk donors results in:

- Increased donor organ utilization
- Improved recipient outcomes
- Improved recipient understanding of risks

Further, few studies have determined what information recipients want to receive about OPTN-defined increased risk donor organs in order to make a decision on whether or not to accept the offer consistent with their individual values and health preferences.

Defining the Optimal Evaluation of Recipients of Organs from Donors at Increased Risk of HIV, HBV, and HCV Transmission

Key Findings and Recommendations
Available data suggests that, despite its low yield, testing of transplant recipients of organs from increased risk donors may identify patients that would benefit from early therapy. Pre-transplant serology should be drawn on such individuals to establish a baseline. Post-transplant, diagnostic tests that directly detect the virus (i.e. nucleic acid tests (NAT) for HIV and HCV and either NAT or HbsAg for HBV) should be utilized. Testing should be conducted at 1 and 3 months post-transplant for HIV, HBV, and HCV and once at a later time point (between 6 and 12 months) for HBV alone. All data on the results of this testing should be collected centrally to allow analysis and to inform future guidance. Screening of all transplant recipients may inform future policy and may detect rare infections, but can only be recommended as a research endeavor at this time.
Identified Gaps in Knowledge

There is very limited data to inform guidance and as a result, research is needed to define the yield and optimal timing of donor screening. Further, given the changing epidemiology of infection, increased travel and the growing population of asymptomatic carriers of HCV, possibly HBV, and other infections, the yield of screening all transplant recipients should be studied. A prospective study of the transmission of infection with organ transplantation in which all donors and recipients were tested (either in real time, retrospectively from banked samples or both) for a fixed period (e.g., 2-3 years), similar to what has been funded for other populations (i.e. REDS).

Acknowledgements

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Invited Members of the conference included:
Working Group 1 – Defining the Increased Risk Donor: Michael Green, MD MPH and Dorry Segev, MD, co-chairs; Michael Abecassis, MD MBA, David Cohen, MD, Williams Hasskamp, Dan Lebovitz, MD, Jeff Orlowski, Peter Reese, MD, David Reich, MD, John Roberts, MD, Michael Volk, MD, and Charles Wright, MD.

Working Group 2 – Live Donor Evaluation: Connie Davis, MD and Chris Freise, MD, co-chairs; Talia Baker, MD, Sandi Cohen, Carrie Comellas, Stuart Flechner, MD, Jami Hanneman, Kevin Korenblat, MD, Dianne LaPointe-Rudow, David Mulligan, MD, Doug Pendrod, and Dorn Sanders.

Working Group 3 – Informed Consent: Emily Blumberg, MD and Rich Freeman, MD, co-chairs; Mark Barr, MD, Mary Amanda Dew, PhD, Nicole Beauvais, James Eason, MD, Robert Gaston, MD, Elisa Gordon, PhD, Doug Hanto, MD, Mitch Henry, MD, Bev Kosmach-Park, Gwen McNatt, and Michelle Vogel.

Working Group 4 – Evaluation of Recipients of Increased Risk Donor Organs: Jay Fishman, MD and Tim Pruett, MD, co-chairs; Peter Abt, MD, Amy Bobrowski, MD, Peter Chin-Hong, MD MAS, Tracy Evans-Walker, Bob Higgins, MD, Dan Kaul, MD, Alan Langnas, MD, Martha Pavlakis, MD, and Stephen Rayhill, MD.
## Table 1. Increased Risk Donor Risk Factor Key Domain as Assessed by Work Group 1 – Definitions Work Group

<table>
<thead>
<tr>
<th>Risk Factor in last 12 months*</th>
<th>Ability to Identify Risk Factor?</th>
<th>Strength of Risk for Infection?</th>
<th>What is estimated Risk?</th>
<th>Proportion of Donors Affected?</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2 sex partners</td>
<td>Very Weak</td>
<td>Weak</td>
<td>Cannot Tell</td>
<td>&gt; 10%</td>
</tr>
<tr>
<td>Sex with known of suspected infected partner</td>
<td>Very Weak</td>
<td>Weak</td>
<td>Cannot Tell</td>
<td>1-5%</td>
</tr>
<tr>
<td>Men who had sex with MSM</td>
<td>Weak</td>
<td>Strong</td>
<td>1:1000 - 1:10000</td>
<td>1-5%</td>
</tr>
<tr>
<td>Women who had sex with MSM</td>
<td>Very Weak</td>
<td>Very Weak</td>
<td>Cannot Tell</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Sex in exchange for money or drugs</td>
<td>Very Weak</td>
<td>Weak</td>
<td>&gt; 1:1000</td>
<td>1-5%</td>
</tr>
<tr>
<td>Sex with someone who had sex in exchange for money or drug</td>
<td>Very Weak</td>
<td>Weak</td>
<td>&gt; 1:1000</td>
<td>5-10%</td>
</tr>
<tr>
<td>Sex with someone who injected drugs for non-medical reasons</td>
<td>Very Weak</td>
<td>Strong</td>
<td>Cannot Tell</td>
<td>1-5%</td>
</tr>
<tr>
<td>Infants ≤ 2 years born to infected mother*</td>
<td>Very Strong</td>
<td>Strong</td>
<td>&gt; 1:1000</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Person who injected drugs for non-medical reasons</td>
<td>Very Strong</td>
<td>Strong</td>
<td>&gt; 1:1000</td>
<td>1-5%</td>
</tr>
<tr>
<td>Intranasal use of illicit drug</td>
<td>Very Weak</td>
<td>Weak</td>
<td>1:10,000 – 1:100,000</td>
<td>1-5%</td>
</tr>
<tr>
<td>Inmate for ≥ 3 Days*</td>
<td>Strong vs Weak?</td>
<td>Strong Vs Weak</td>
<td>1:1000-1:10,000</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Person treated for syphilis, gonorrhea or genital ulcers</td>
<td>Very Weak</td>
<td>Weak</td>
<td>Cannot Tell</td>
<td>&gt; 10%</td>
</tr>
<tr>
<td>Person on hemodialysis</td>
<td>Very Strong</td>
<td>Strong</td>
<td>&gt; 1:1000</td>
<td>1-5%</td>
</tr>
<tr>
<td>Immigration to US from country with higher HBV prevalence</td>
<td>Very Strong/Strong</td>
<td>Weak/Very Weak</td>
<td>Cannot Tell</td>
<td>&lt; 1%</td>
</tr>
</tbody>
</table>