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

Principal Investigator: Michael G. Ison, MD MS¹, ²

Team Members: Michael Abecassis, MD MBA,² Emily Blumberg, MD,³
Connie Davis, MD,⁴ Jay A. Fishman, MD,⁵ Richard B. Freeman, MD,⁶
Chris E. Freise, MD,⁷ Michael D. Green, MD MPH,⁸ Dorry Segev, MD,⁹
Tim L. Pruett, MD¹⁰

¹Division of Infectious Diseases and ²Organ Transplantation, Northwestern University Feinberg School of Medicine, Chicago, Illinois, ³Division of Infectious Diseases, University of Pennsylvania, Philadelphia, Pennsylvania, ⁴Division of Nephrology, University of Washington, Seattle, Washington, ⁵Division of Infectious Diseases, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts, ⁶Department of Surgery, Geisel School of Medicine, Dartmouth University, Hanover, New Hampshire, ⁷Division of Transplant Surgery, University of California at San Francisco, San Francisco, California, ⁸Divisions of Pediatric Infectious and Transplant Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, ⁹Division of Transplant Surgery, Johns Hopkins University, Baltimore, Maryland, ¹⁰Division of Transplantation, University of Minnesota, Minneapolis, Minnesota

Organization: Northwestern University Feinberg School of Medicine


Federal Project Officer: Carol Harris

Acknowledgement of Agency Support: This project was supported by a R13 grant from the Agency for Healthcare Research and Quality.

Grant Award Number: AHRQ 1R13HS021060-01
Structured Abstract

Purpose: To review the existing evidence and identify gaps about defining donors at increased risk of transmission of HIV, HBV, and HCV, the evaluation of living donors to mitigate against infectious disease transmission, the optimal timing, content, and method of informed consent of candidates considering an increased risk donor organ and the optimal evaluation of recipients of organs from an increased risk donors.

Scope: Transplant experts were invited to participate in the 4 workgroups.

Methods: The workgroups reviewed the evidence to support recommendations and identify gaps in knowledge for their topic. Their findings were discussed and consensus about the topics was made at an meeting held on April 27, 2012.

Results: The group reviewed the identified risk factors for HIV, HBV and HCV. Definitions should focus on risk factors that occur in <10% of the donor population, represent a significant risk of infection (>1:10,000 donors) and can be assessed reliably. All live donors should be screened for risk behaviors for HIV, HBV and HCV and be educated on how to avoid contracting these infections prior to organ procurement. All live donors should be screened within 30 days (preferably within 14 days) prior to surgery by HIV NAT, HBsAg, and HCV NAT to detect acute infection prior to donation. Despite its low yield, testing of recipients of increased risk donor organs may identify patients that would benefit from early therapy. Post-transplant diagnostic tests that directly detect the virus should be utilized.

Key Words: Donor-Derived Infection, HIV, HBV, HCV
Purpose
The purpose of this project was 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 would identify gaps in current knowledge on these issues that, in the opinion of the transplant community, need further research to inform future policy and practice.

Scope
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 (1-3). 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”) (4, 5). 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 (6-9). OPTN policy and CMS guidelines also requires special informed consent from candidates before transplanting organs from such increased risk donors, although specifics about how to conduct such consents has not been defined (2, 5). 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 (1, 6, 10).

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.

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.

Methods
Prior to the release of the proposed revised USPHS Guideline for Reducing Transmission of HIV, HBV, and HCV through Solid Organ Transplantation, a R13 proposal was drafted and submitted to AHRQ with the goals of reviewing the current research findings and identifying gaps in the evidence related to the 4 key topics of this conference, as listed above. Once the proposal was funded, the principal investigator invited to the American Society of Transplant Surgeons and the American Society of Transplantation to serve as co-sponsor for the meeting.
Both societies accepted this invitation. In addition, all members of the transplant community were invited to attend the meeting, which was open to the public.

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.

Results
Establishing a Consensus Definition of Donors at Increased Risk of Transmission of HIV, HBV, and HCV
The existing PHS guideline that was published in 1994 and is the basis of the current OPTN definitions of increased risk donors was initially developed to only prevent the transmission of HIV.(4) This guideline is currently in the process of being revised with a broader goal that now includes generating updated evidence-based criteria which will identify donors at increased risk of transmitting HIV, HBV and HCV. The process has inherent limitations in accomplishing its goal due to the lack of relevant data in the literature. Specifically, only 30 publications met criteria for inclusion in the evidence review relevant to these “new” definitions despite expansion of the literature review to include potential tissue donors, blood donors and the general population. Only 2 of the 30 publications included data on risk that potential or actual organ donors carry HIV, HBV or HCV and only 2 specifically assessed pediatric donors.
In approaching the goal of defining donors at increased risk for disease transmission, several potential philosophical approaches could be considered, including:

- Maximally reduce risk of transmission by excluding donors which would have a clear impact by reducing the number of acceptable donors.
- Minimizing risk of inadvertent transmission to the lowest possible level by using a list of criteria with high sensitivity. Such an approach must recognize that use of higher sensitivity can result in greater lack of specificity. Further, implementing this approach will likely result in uninfected donors being incorrectly labeled as increased risk, which may affect utilization of organs from such a donor. Such donors would not be excluded from donation.
- Maximizing the specificity of definitions for which donors are at risk of transmission. Such an approach increases the likelihood of missing the presence of infection with HIV, HBV or HCV in some potential donors and accordingly result in an increased potential risk of unexpected transmission to recipients, potentially impacting on public perception of the safety of organ transplantation. To counterbalance this risk, patients are more likely to receive organs in a shorter period of time with the potential to improve quantity and quality of life in the recipients.

In determining where to set the balance between sensitivity and specificity, one needs to identify the acceptable risk of transmission. To do this, it is critical to understand if the probability of transmission from a donor known to be infected varies depending on the pathogen present. Further, current laws (NOTA) and policy forbids the use of HIV infected donors but permit the use of HBV and HCV infected donors in certain circumstances. The Working Group identified 4 key domains which were used to categorize each of the 14 behavioral risk factors proposed in the draft version of the PHS Guidelines submitted for public comment in 2011. These domains determined IF each risk factor was reliable in predicting a higher likelihood that a donor would carry an infection with HIV, HCV or HBV that would not be detected with routine serology,, and finally, estimated what percent of the donor pool might be expected to have one of these risk factors. Based on this assessment, the work group voted whether each of the 14 proposed risk factors should be included as a reliable indicator of an increased risk for incident (i.e. window period) donor infection with HIV, HBV or HCV.
Gaps in Knowledge Related to Defining Donors at Increased Risk of Disease Transmission
After reviewing the literature, it was clear that there were significant gaps in knowledge required to more accurately define organ donors at increased risk of transmitting HIV, HBV or HCV. Specifically, there was limited data on actual residual risk of HIV, HBV and HCV drawn from organ donors.

Defining the Optimal Evaluation of Living Donors to Mitigate Against Transmission of HIV, HBV, and HCV
Screening of live donors is essential to minimize the risk of transmitting disease from the donor to the transplant recipient. In data reported to the OPTN since 2006, there have been 15 reports of potential disease transmissions from a live donor to a recipient (8 involving malignancies and 7 involving infections; 6 were initiated from disease discovered post-transplant in the recipient and 9 from disease discovered post-transplant in the donor). There are currently several different guidance documents related to the optimal evaluation of live donors for organ transplantation available; most reflect general screening recommendations without providing specific timelines for when screening should be performed. In response to the recent transmission of HIV from a live donor, the Centers for Disease Control and the NY Department of Health have issued more specific donor screening recommendations. These guidelines recommend repeat serology and NAT of donors within 7 and 14 days of the transplant procedure, respectively.

There are differences in the screening of live donors as compared to deceased donors. Since live donation is generally an elective procedure, there is sufficient time to perform any test that is felt appropriate by the transplant team. Such time allows for repetition of tests to determine if results are falsely positive. Unfortunately, the extra time may also permit the donor to engage in activities that results in acquisition of infection in the time period between their screening assays and the transplant procedures. Lastly, the live donor can provide information about their own
risk behaviors and can be educated on how to avoid contracting certain infections between evaluation and transplantation.

The work group surveyed transplant administrators about their current practice for screening live donors to calibrate recommendations with current practice. Seventy-two individuals responded to the electronic survey. Of note, few of the responding centers (18.3%) have changed their donor screening protocols in response to the CDC and NY state DoH recommendations; 58% percent of those who did make changes screen for HIV and HCV within 7 days while 42% of those who did not make changes, screen for HIV and HCV within 7 days; a further 27.4% repeat testing at some point beyond 7 days. Most centers (72.5%) discuss minimizing risk behaviors, typically at the donors first evaluation.

To inform their recommendations, existing studies of epidemiology and guidelines for screening individuals for HIV, HBV and HCV were reviewed in detail. The extensive work prepared by the donor testing work group from a prior live donor consensus conference was also reviewed in detail.

*Recommendations Agreed Upon by Attendees*

Based on review of existing literature, 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 prevalent 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. In addition, the working group recommended that all
live donors, irrespective of risk status, should be screened within 30 days but preferably within 14 days of donation by HIV, HBsAg, and HCV NAT to improve the likelihood of detecting an acute infection acquired in the immediate time prior to donation.

Gaps in Knowledge Related to Live Donor Screening
There are many gaps in our understanding of how to screen live donor to prevent disease transmission. There are limited data on the cost of implementation of the various testing strategies. Likewise, there are limited data assessing historical or laboratory testing accuracy, the frequency of true positive results and the incidence and risk factors for false positive results of testing living donors. The workgroup was also concerned that there is almost no assessment of what psychological and financial impact that a false positive screening test might have on the donor or donor family. Furthermore, since FDA-approved, licensed or cleared screening assays may not be available at all live donor transplant centers, some centers have developed their own PCR based assays for HIV, HCV and HBV and the test characteristics and yield, including false positive and negative results, of both the FDA-approved and “home brew” assays for quantitative and qualitative PCR for HIV, HBV and HCV have not been well delineated when used to screen living donors. Lastly, there are concerns regarding potential delays in living donor transplantation that might be introduced because of false positive test. This may have serious consequences for paired donor exchange and living donor chain transplants. The frequency and impact of this problem has not been addressed to date. 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
CMS and the OPTN require that candidates for organ transplantation be informed of risks that may affect the outcome of transplantation, including donor risk factors that could affect either
the function of the allograft or the recipient’s health. These requirements include general
guidance for areas that need to be addressed during the informed consent process. Although
the components of consent are outlined, there is no specific recommendation for how the
consent process should be conducted and documented. Although this conference focused on
the increased risk donor, The meeting attendees agreed that the consent process should
encompass the diversity of risks associated with transplantation and should not be restricted to
donor transmission events. Some attempt to compare and contrast the various risks and
probabilities should be made to put these all into context for the potential recipient.

To date, there has been limited research on the informed consent process related to accepting
organs from donors who may be carrying an increased risk of transmitting HIV, HBV and HCV.
The few available studies have assessed how patients make decisions related to accepting
organs from sub optimal donors. Lessons learned from this research can help to improve the
consent process by which candidates are informed about the risks of utilizing organs from
donors who may have increased risks for transmitting HIV, HCV, or HBV (11, 12). In one study,
the investigators assessed patients’ information needs and misunderstandings about the
magnitude of risks increased risk donors carry and suggested that these should be addressed in
order to better education potential recipients and improve the consent process.(13) From data
from other studies, it may be possible for patients to better understand the risks they are being
asked to take and contextualize these risks with others they are accepting with undergoing a
transplant, such as graft dysfunction, malignancy, and other infections (14). Further, some have
questioned the optimal timing of obtaining patients’ informed consent (15).

From the existing data, there are several general principles that should be considered in
obtaining informed consent from a patient for organs from a donor with risk factors for HIV, HBV
and HCV:
• The informed consent process for increased risk donor organs has shortcomings.
• There are limitations to the donor historical information and laboratory testing, which should be clearly communicated to potential recipients.
• Although each institution will have its own language to be included in the documentation around informed consent for procedures, the conference attendees agreed that the presence of the written documentation is necessary but not sufficient for ensuring an adequate and shared consent process.
• Since not all patients prefer to take full responsibility for their decision-making process, patients should be encouraged to seek additional resources if needed (13).
• A clear distinction between the risk of disease transmission and other risks of such as primary graft failure, early graft dysfunction, reduced graft function time, rejection and other organ and donor derived parameters likely to affect to overall outcome of the transplant should be discussed (13). It should be made clear that the donor factors that may indicate an increased risk of disease transmission are likely to be different than the factors that may immediate or long-term graft function.
• Specific information about risk of undetected infection in the donor should be discussed in terms that the patient understands using the best possible data available (13, 16, 17).
• The potential benefits of accepting an increased risk donor organ should be described. These include saving lives, increasing longevity, reducing the risks of other complications of ongoing therapies (including dialysis), improved health and quality of life, and expansion of the donor pool with reduction in the waiting time.
• Potential risks of not accepting the organ, including the option to be offered organs at a later time, should be discussed with the patient.
• Risk should be explained in terms that the patient can understand, using plain language and health communication best practices that facilitate comprehension in patients regardless of their individual educational level.
• Concerns of living donors need to be included in these discussions and anytime a donor starts to feel uncomfortable about the implications to their job, family or future care they should be given the option to opt out of donation.
• All of these risks must be weighed for the individual patient’s specific circumstances to promote tailored treatment decision-making.

Recommendations Agreed Upon by Attendees
In reviewing the available literature on informed consent for increased risk donors and broader literature on general principles of consent in transplantation and related fields, the attendees agreed upon a range of minimal recommendations for obtaining informed consent from individuals being offered organs from increased risk donors. In general, live donors should allow disclosure of their relevant medical and social information to the potential recipient in order to provide the recipient with a clearer understanding of the risk. The consent process should, in general, be the same when a candidate is considering organs from an increased risk live or deceased organ donor (i.e. there should be multiple encounters where the risks of
transplantation including disease transmission are discussed with the potential recipient to allow for a shared decision-making process). Education about donor factors that could increase the probability of transmitting HIV, HBV or HCV 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 process should be conducted by knowledgeable, trained clinicians who can answer specific questions about the risks posed. The discussion of risk should be described as a continuum with issues related to donor derived infection with HIV, HBV and HCV placed in context of all risks associated with transplantation. At the time of the organ offer, the consent process 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.

Gaps in Current Knowledge Related to Informed Consent
After reviewing the existing literature, few studies were available that addressed the optimal timing, content, and method of disclosing information and obtaining informed consent from candidates considering accepting organs from donors with risk factors for carrying HIV, HBV, and HCV. Although it is possible to extrapolate from studies of consent in other clinical situations, further research is needed to improve the process by which consent for the use of organ from donors with increased risks. Specifically, little is known as to whether requiring special informed consent by candidates accepting organs from donors thought to carry increased risks 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**

From 2007 – 2010, there have been 60 investigations where HIV, HBV, or HCV was specifically suspected as being acquired from the donor, it is likely that disease transmission occurs more often than recognized or reported (5). Additionally, there are no prospective studies of disease transmission in transplantation. Thus, the baseline incidence of infection in the general and increased risk populations must be imputed from studies of blood transfusion and epidemiologic studies. In order to identify donor-derived infections before the development of clinical disease, a few features of testing must be considered:

1. Diagnostic tests must be used (as opposed to screening assays) – these will, in general, be approved by the FDA for diagnostic use. Nucleic acid tests (NAT) are preferred given the potential for delayed or absent seroconversion in immunosuppressed transplant recipients.
2. Reported transmission events have usually resulted in clinical disease early in the post-transplant course; generally within 1-2 months.
3. Greatest risk for donor-derived infection is for unknown or uncommon pathogens (not HIV, HCV, HBV) or those resistant to common antimicrobial prophylaxis.
4. The core question is whether asymptomatic disease transmission of HIV, HCV and HBV can be recognized in advance of symptomatic disease? In the immunosuppressed host, viral replication and disease progression are generally more rapid than in immunologically normal hosts. Clinical disease for HIV, HCV, and HBV is expected to occur by 6 months after transplantation – with the expectation that viremia is established earlier. There is some risk that community acquisition of new disease unrelated to the transplant exposure may occur the longer out the recipient is from transplant surgery.
5. There are no data in the non-transplant populations to indicate that "early therapy" (weeks to months) is clinically advantageous with the exception that all therapy for HBV and HCV must be initiated before the development of cirrhosis. One potential advantage to early diagnosis might be avoidance of inadvertent transmission to uninfected social and sexual partners.
6. It is important to distinguish between a virologic diagnosis (i.e., viremia) and clinical or symptomatic disease (hepatitis or AIDS). Symptomatic progression is expected to be more rapid in immunosuppressed hosts. A reasonable testing paradigm would include testing of recipients of organs from “donors at increased risk for transmission of infection” pre-transplantation (baseline) and at 1 and 3 months after transplantation using a diagnostic NAT assay with high sensitivity (10-25 IU/ml cutoff). Testing at later time
points (6 months to 1 year) would capture late HBV infection. It is not known whether these individuals become viremic before those time points.

Given the great variability in viral strains, viral loads, organ manipulation (e.g., flushing that may remove leukocytes and blood), carriage of virus by different organs, and differential effects of various immune suppression regimens on transmission, the diagnostic assays deployed after transplantation must assume the worst case scenario diagnostically: low level of virus, slow seroconversion or delayed viral replication.

The 1994 US PHS guidelines recommend recipient screening at 3 months post-transplant; a more recent expert panel recommended screening at 1, 3, and 12 months post-transplant. Nonetheless, implementation of these recommendations has been poor. As of 2007, far less than 50% of surveyed transplant centers routinely screened recipients of organs from increased risk donors for HIV, HBV, and HCV post-transplant despite the reduced sensitivity of serologic diagnosis, especially for HCV.

The group reviewed existing data to determine the expected time from transplant to the development of clinically-symptomatic HIV, hepatitis B and hepatitis C infection and the impact of early antiviral therapy on long-term clinical outcomes. Donor-derived HIV infection appears to result in a rate of progression that is much more rapid than in non-immunosuppressed individuals. Further, early therapy is currently recommended by current treatment guidelines and therapy should be considered for non-transplant patients with seroconversion in the previous 6 months. Although the timing of initially detectable viremia post-transplant is not well studied, existing data support early diagnosis and treatment. Clinical symptoms of acute HBV disease in HBV naïve solid organ recipients were reported at 2-39 months. Although the data on outcomes of early treatment of acute HBV in transplant recipients is sparse, patients who are at higher risk for developing more severe disease can be treated with antivirals. In general,
viremia can be detected early (weeks) using NAT assays while liver function abnormalities may take longer to develop. HCV infection of naïve liver recipients (new hepatitis) has been associated with a 55.1% five year survival. Quantitative NAT is useful for guidance of therapy and highly sensitive assays (10-25 IU/ml cutoff) should be used for diagnosis of possible infection. Optimal timing of treatment is unknown; risk of rejection and treatment toxicity may be more significant with early treatment and there are no studies to document its benefit. This may change with the introduction of less toxic and more effective directly acting antiviral agents (DAA).

**Recommendations Agreed Upon by Attendees**

In summary, this data suggests that, despite its low yield, testing of transplant recipients of organs from increased risk donors may identify patients who may benefit from early therapy to prevent further transmission and improve outcomes. 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. Results of this testing should be collected centrally to allow analysis and to inform future guidance. Post-transplant 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.

**Gaps in Current Knowledge**

Unfortunately, there is very limited data to inform guidance and as a result, research is needed to define the yield and optimal timing of recipient 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 potential yield of screening all transplant recipients, as compared to the current paradigm of only screening recipients of organs from...
OPTN-defined increased risk of infection, should be studied, including cost effectiveness of various strategies. Funding for 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) would significantly improve the knowledge base in this area.
## Table 1. Consensus Recommendations Approved by the Attendees of the Conference

<table>
<thead>
<tr>
<th>Work Group</th>
<th>Consensus Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WG 2: Live Donor Screening</strong></td>
<td>• All live donors should be screened for risk behaviors for HIV, HBV and HCV as defined by this conference</td>
</tr>
<tr>
<td></td>
<td>• Pre-transplant serology for HIV, HBV and HCV should be collected at any time point in the donor evaluation process</td>
</tr>
<tr>
<td></td>
<td>• All live donors should be screened within 30 days but preferably within 14 days prior to surgery by HIV NAT, HBsAg, and HCV NAT*</td>
</tr>
<tr>
<td></td>
<td>• All live donors should be educated on how to avoid contracting HIV, HBV and HCV at any point between evaluation and donation</td>
</tr>
<tr>
<td><strong>WG 3: Informed Consent</strong></td>
<td>• Live donors should be consented to allow disclosure of their relevant medical and social information to potential recipients°</td>
</tr>
<tr>
<td></td>
<td>• Risk should be described as a continuum with the donor issued placed in context of all risks associated with transplantation</td>
</tr>
<tr>
<td></td>
<td>• Recipient consent process should be the same for live and deceased organ donors</td>
</tr>
<tr>
<td></td>
<td>• Consent should be obtained by knowledgeable, trained personnel</td>
</tr>
<tr>
<td></td>
<td>• Consent should be comprehensible to recipient, utilizing format and language appropriate to the individual recipient and include risk and post-transplant testing</td>
</tr>
<tr>
<td></td>
<td>• The recipient’s social support (family, significant others, etc...) should be encouraged to be involved in the consent process</td>
</tr>
<tr>
<td></td>
<td>• Education about increased risk donors should be provided at 2 discrete times: Prior to listing and at the time of the organ offer</td>
</tr>
<tr>
<td></td>
<td>• Reinforcement of education should be made throughout the waiting period</td>
</tr>
<tr>
<td></td>
<td>• The informed consent process should protect the donor and recipient confidentiality</td>
</tr>
<tr>
<td></td>
<td>• The process for each consented individual should be documented by the transplant center</td>
</tr>
<tr>
<td></td>
<td>• There is a need to develop an educational tool for training professionals delivering consent discussion</td>
</tr>
<tr>
<td><strong>WG 4: Recipient Testing</strong></td>
<td>• Nucleic acid tests (NAT) are preferred for HIV and HCV (HBsAg adequate for HBV)</td>
</tr>
<tr>
<td></td>
<td>• All recipients of organs from “donors at increased risk for transmission of infection” should be tested:</td>
</tr>
<tr>
<td></td>
<td>o Pre-transplant to obtain a baseline and 1 and 3 months after transplant</td>
</tr>
<tr>
<td></td>
<td>o Additional testing between 6 and 12 months just for HBV</td>
</tr>
<tr>
<td></td>
<td>• All data on these test results should be collected centrally</td>
</tr>
</tbody>
</table>

*29 (74%) attendees voted to recommend testing by HIV NAT, HBsAg and HCV NAT prior to surgery (the 10 individuals who opposed the recommendation cited questions of the risk/benefit ratio, the potential of loss of donors and/or donor-recipient pairs and enhancing fear in the donors). Although the majority (21 (54%) attendees) voted in favor of screening within 30 days but preferably within 14 days, 18 (46%) initially voted to recommend testing within 14 days and 7 (18%) initially voted to recommend testing within 7 days of the transplant procedure.

°5 (13%) attendees voted against this recommendation
Table 2. Identified Gaps in Knowledge Related to Increased Risk Donors

- Limited data on the optimal screening of live and deceased donors for HIV, HBV and HCV. A prospective study could be designed to determine how many donors were positive by antibody and NAT at different timing to assess the relative yield of screening.
- There is currently no data on post-transplant screening results of recipients of standard and increased risk donor organs to assess the incidence of donor-derived disease transmission. A prospective study which tested recipients at fixed intervals post-transplant could inform optimal recipient screening and yields.
- Assessment of the cost of implementation of testing by serology and/or NAT in live and deceased organ donors.
- Potential factors related to false positive serologic and nucleic acid testing results for live and deceased organ donor screening.
- The number and impact of false positive tests on the number of transplants performed, recipient transmissions, wait list time and potential donor psychological, medical and financial outcomes.
- Assessment of yield and false positive and negative results if FDA-approved, licensed or cleared diagnostic or monitoring NAT assays were utilized for live and deceased donor screening.
- There is limited data of the impact of the informed consent process on transplantation, especially with regard to use of increased risk donors.
- There are currently no standardized tools to assess comprehension of the informed consent in transplantation, particularly with regard to the use of organs from an increased risk donor.
- There is currently limited data on how best to tailor the content and level of detail of consent from the patients point of view (patient-centered consent) with regard to the use of organs from an increased risk donor.
- There is a need for a decision analysis which quantitatively weighs the magnitude of harm associated with window period infections against the magnitude of unused organs. Such analysis would have to take into account that variations in utilization of organs by identified risk, accepting center, and type of organ being transplanted.
- There are currently limited data to address the strength of risk for unsuspected window period infection for many of the potential risks which limits the ability to assess the net value of including the risk factor.
- Can we identify more precisely the “times” associated with proposed risks to enhance their specificity to identify window period infections?
- Incidence studies of people in various putative risk groups, particularly those where high-- quality incidence studies do not currently exist.
- Expanded national data collection on the specific risk factors underlying “CDC high risk” designation.
- Studies of patient attitudes, concerns, and priorities regarding infectious risk and the specific categories used to define higher infectious risk.
- Improvements in efficiency, accuracy, and availability of nucleic acid testing.
- Better quantification of false-- positive rates of nucleic acid tests.
- National consensus and homogeneity among OPO’s regarding nucleic acid testing methods.
- Comparative Risk analysis: between risk of infection and risks of turning down an organ or donor withdrawing (i.e. no transplant).
List of Publications and Products

A draft paper will be submitted to the *American Journal of Transplantation*.

All slides and recommendations derived from the meeting can be found on-line at:
http://www.feinberg.northwestern.edu/transplant/Increased%20Risk%20Consensus%20Conference/

References


