Curr Transpl Rep (2016) 3:57–63
DOI 10.1007/s40472-016-0087-8

OPTN POLICY (K ANDREONI, SECTION EDITOR)

Changing the US Public Health Service Guideline for Reducing Viral Transmission Through Organ Transplantation

Michael G. Ison [1,2]

Published online: 26 January 2016

Abstract In response to several inadvertent transmissions of human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) through organ transplantation, the US Public Health Services issued guidelines to prevent the transmission of HIV through transplantation of human tissue and organs in 1994. Despite significant changes in the epidemiology of HIV in the USA and advances in screening assays for detecting latent infection, the guidelines remained generally unchanged for nearly 20 years. Although the 1994 guidelines identified risk factors in donors that placed them at increased risk of HIV transmission, compliance with the recommendations was highly variable at US transplant centers. After the cotransmission of HIV and HCV from one donor to four transplant recipients, the OPTN policies were amended to incorporate the definitions of donors at increased risk for HIV and required transplant centers to obtain specific informed consent and follow-up when such donor organs were utilized. With renewed attention, it became obvious that the guidelines needed to be revised and expanded to include HBV and HCV. A revised US PHS Guideline was developed over a several year period, and final recommendations were published in 2013. Despite the revisions, definitions of donors at increased risk of disease transmission require further review and revision. This article will attempt to review the revision process of the US PHS Guideline and make suggestions for next steps in further refining the guideline.

Keywords Human immunodeficiency virus (HIV) · Hepatitis B virus (HBV) · Hepatitis C virus (HCV) · US Public Health Service (US PHS) · Increased risk donor

This article is part of the Topical Collection on *OPTN Policy*

✉ Michael G. Ison
mgison@northwestern.edu

[1] Divisions of Infectious Diseases and Organ Transplantation, Northwestern University Feinberg School of Medicine, 645 N. Michigan Avenue, Suite 900, Chicago, IL 60611, USA

[2] Northwestern University Transplant Outcomes Research Collaboration, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Introduction

Ever since human immunodeficiency virus (HIV) was initially identified in the early 1980s, its ability to be transmitted by blood, organ, and tissues has been evident. Beginning in 1983, prospective blood donors who engaged in risk behaviors for HIV infection were excluded from donating blood [1•]. Once serologic tests for HIV antibodies were approved in 1985, screening of prospective blood, organ, and tissue donors began [2, 3]. This screening resulted in significant reductions in the rate of transmission of HIV via these routes. Despite this screening, rare transmissions of HIV continued to occur [4–6, 7••]. A high-profile transmission of HIV from one organ and tissue donor to 7 of 58 recipients of heart, liver, and 2 kidneys in addition to recipients of 2 femoral head and patella transplantations resulted in the first US Public Health Service (PHS) guideline related to preventing the transmission of HIV through organ and tissue donation; the donation event occurred in 1985 and was first recognized in 1991 [7••, 8••].

To prepare the first US PHS guideline, a working group was formed with representatives from several federal agencies with oversight over organs and tissues, donor screening tests, and the epidemiology of HIV/AIDS. A panel of external consultants from interested parties, including key public and private health professionals, as well as key government agencies

(Centers for Disease Control and Prevention, Food and Drug Administration, Health Care Financing Administration, Heath Resources Services Administration, the National Institutes of Health and the Office of the Assistant Secretary for Health) was also constituted to independently review the guideline and provide advice to the US PHS to optimize the guideline. These guidelines were developed in the context of a desire to reduce the risk of transmission of HIV through organ and tissue donation in an era where there was significant stigma around HIV and low rates of testing and early detection of HIV infections in the US population. Additionally, the guidelines were developed with earlier generations of HIV antibody testing that had a relatively long window period, of up to 4–10 weeks [9]. Based on these assumptions and limitations, the guidelines recommended that "persons who meet any of the criteria, listed in Table 1, should be excluded from donation of organs or tissues unless the risk to the recipient of not performing the transplant is deemed to be greater than the risk of HIV transmission and disease (e.g., emergent, life-threatening illness requiring transplantation when no other organs/tissues are available, and no other life-saving therapies exist). In such a case, informed consent regarding the possibility of HIV transmission should be obtained from the recipient [8••]."

There was concern from the transplant community that the guideline would significantly harm the field by excluding many donors that could safely be used for organ transplantation. As such, the guideline had the potential to result in more harm, through patients not being transplanted, than benefit. In response to these concerns, the Centers for Disease Control issues a clarification that stated that "when a potential organ donor tests HIV-antibody negative but has behavioral risk factors for HIV infection, the decision to accept an organ for transplantation should be made after consideration of the relevant risk factors for the individual recipient and with recognition of the very low incidence of HIV transmission in such situations. CDC recognizes the need for transplant centers, not organ procurement organizations, to deal with matters of patient consent in this setting [10]." With this clarification, the basic tenants of prevention transmission through organ transplantation included the following:

- A list of factors that place donors at increased risk of having HIV infection
- Transplant centers should carefully review the available donor information to assess the risk of undiagnosed HIV and contextualize that risk with the risk of adverse consequences of the recipient not undergoing an organ transplantation
- The transplant center should obtain special informed consent from the potential recipient or their appointed decision maker prior to accepting the organ
- The transplant center should test the recipient for acquisition for HIV from the donor with a recommended time of screening of 3 months post-transplant

These guidelines were clearly published, but compliance with the recommendations was not clearly assessed. The Organ Procurement and Transplant Network (OPTN) did not enact policy related to these guidelines, and therefore, the OPTN had no mechanism to assess compliance with the guideline. Nonetheless, evidence suggests that key components of the recommendations were not universally followed. A survey of Transplant Infectious Diseases experts performed in 2007 attempted to assess compliance with the recommendations of the guideline [11•]. While the response rate was low and limited to Transplant Infectious Diseases clinicians, the authors hypothesized that this would be a population more likely to understand the guidelines and operationalize the recommendations. Thirty-three percent of responding centers obtain only verbal, 52 % verbal and written, and 14 % do not obtain any special consent from recipients of organs from increased risk donors (ROIRD). Post-solid organ transplantation serologies for HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) are obtained at 40 % of centers in ROIRD only, 20 % in all recipients, and not performed in 40 %. Post-solid organ transplantation nucleic acid testing (NAT) testing is carried out in 36–45 % of centers in ROIRD, 11 % in all recipients, and not performed in approximately 50 % of centers [11•]. The study also attempted to investigate how frequent results were reported to the OPTN as required by recipient data collection tools. Because of changes in data collection by UNOS related to increased risk status and HIV and HCV testing results post-transplant, only data from June 30, 2004, to February 28, 2006, for thoracic organs and to August 31, 2006, for abdominal organs were available. Additionally, because of local and state laws related to reporting of HIV results, not all HIV results could be captured by UNOS. The available data, though, show a very low rate of post-transplant testing, at any time point, for HIV and HCV in recipients of increased risk donor organs: 3.7 % had reported HIV results and 5.9 % have reported HCV results [11•].

The transplant community applied renewed attention to the approach to increased risk organ donors after a cotransmission of HIV and HCV from one seronegative, appropriately labeled increased risk organ donor to four (two kidneys, liver and heart) recipients in 2007 [12••]. In this case, the donor's only known risk factor for HIV was having sex with another man. Nonetheless, retrospective testing confirmed that the donor was truly seronegative but positive by nucleic acid testing (NAT). The HIV nucleotide sequences were indistinguishable between the donor and four recipients, and HCV subgenomic sequences clustered closely together. As the result of this transmission event, the OPTN quickly put policy into place that codified the "Exclusionary Criteria" from the 1994 PHS

Table 1 1994 US PHS guideline donor exclusion criteria

Criteria	Characteristics
Behavior and history	1. Men who have had sex with another man in the preceding 5 years.
	2. Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years.
	3. Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates.
	4. Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years.
	5. Persons who have had sex in the preceding 12 months with any person described in items 1–4 above or with a person known or suspected to have HIV infection.
	6. Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or mucous membrane.
	7. Inmates of correctional systems.
Pediatric donor	1. Children meeting any of the exclusionary criteria listed above for adults should not be accepted as donors.
	2. Children born to mothers with HIV infection or mothers who meet the behavioral or laboratory exclusionary criteria for adult donors (regardless of their HIV status) should not be accepted as donors unless HIV infection can be definitely excluded in the child as follows: Children >18 months of age who are born to mothers with or at risk for HIV infection, who have not been breast fed within the last 12 months, and whose HIV antibody tests, physical examination, and review of medical records do not indicate evidence of HIV infection can be accepted as donors.
	3. Children ≤18 months of age who are born to mothers with or at risk for HIV infection or who have been breast fed within the past 12 months should not be accepted as donors regardless of their HIV test results.
Laboratory and other	1. Persons who cannot be tested for HIV infection because of refusal, inadequate blood samples (e.g., hemodilution that could result in false-negative tests), or any other reasons.
	2. Persons with a repeatedly reactive screening assay for HIV-1 or HIV-2 antibody regardless of the results of supplemental assays.
	3. Persons whose history, physical examination, medical records, or autopsy reports reveal other evidence of HIV infection or high-risk behavior, such as a diagnosis of AIDS, unexplained weight loss, night sweats, blue or purple spots on the skin or mucous membranes typical of Kaposi's sarcoma, unexplained lymphadenopathy lasting >1 month, unexplained temperature >100.5 F (38.6 °C) for >10 days, unexplained persistent cough and shortness of breath, opportunistic infections, unexplained persistent diarrhea, male-to-male sexual contact, sexually transmitted diseases, or needle tracks or other signs of parenteral drug abuse.

Source: [8••]

guidelines as increased risk criteria for donors. Further, OPTN policy required obtaining special informed consent from recipients willing to accept organs from such increased risk donors. About a year later, policy was further amended to require transplant centers to perform appropriate testing of recipients to assess for transmission of infection.

Although the OPTN requires special informed consent from recipients who agree to accept organs from increased risk donors, there are limited data on what should be shared with the recipients and how best to discuss the sensitive topic. This is critical because accurate, easily understandable information is needed to allow the patient to make a truly informed decision. Further, the data needs to be given to the patient in such a way that they can easily contextualize the risk with the alternatives, including not undergoing transplantation. This is especially important as just hearing that a donor "may" have HIV or hepatitis may result in the patient rejecting the organ offer even though the risk of the alternative (i.e., dialysis) may be higher than accepted an organ from a donor with risk factors [13]. Further, data from surveys of patients suggest that patients confuse risk posed by OPTN-defined increased risk donors and other nonstandard risk donors, such as deceased after cardiac death or extended criteria donors [14]. As such, they may misunderstand the risk posed by the donor organs and turn down the offer. This challenge is especially difficult in living donation in which there may be some connection between the donor and recipient [15].

One of the first steps in providing meaningful informed consent is to assess the residual risk of an undiagnosed HIV or hepatitis C virus (HCV) infection in a donor screened with

serologic or serologic plus nucleic acid testing (NAT). From a meta-analysis of existing literature, it became clear that the risk of residual HIV and HCV infection was reduced with serology plus NAT compared to serologic testing alone, generally by a log (see Table 2) [16••, 17••]. These studies also demonstrated significant variability in the residual risk based on the specific behavioral risk factor present in the donor (see Table 2) [16••, 17••]. For even the highest risk behavior, nonmedical injection drug use, the residual risk of HIV and HCV with serology plus NAT screening is similar to the risk of acquiring HIV or HCV on dialysis for 1 year in the USA. As such, these data provide useful tools to contextualize the risk for patients and allow for more informed decision making by the patient.

With the new OPTN requirements in response to the HIV-HCV cotransmission event, the transplant community also recognized that the PHS guidelines needed to be updated. This led to calls from the transplant professional societies, the Advisory Committee on Organ Transplantation, and others for a revision and updating of the guideline. Since there were a number of transmission events of HBV and HCV involving donor organs, it was felt that the guideline should be expanded to include these two viruses as well [12••, 18–21]. Further, with a transmission of HIV through living organ donation, it was also determined that the guideline should provided greater clarity about live organ donors [22•]. Lastly, it was determined that the guideline utilized factors known to be associated with an increased likelihood of recent HIV, HBV, or HCV infection as a surrogate for determining which donors should be classified as at increased risk of disease transmission.

The primary goal for this revision was to make the guideline as strongly evidenced-based as possible. To do so, the guideline was crafted through a interagency working group of the US PHS with outside support for a systematic review by an independent academic group (The University of Pennsylvania Center for Evidence-Based Practice), three experts to provide expert opinion for issues with limited published evidence, and two external advisory committees who provided comments and advice to strengthen the guideline and attempt to make it more clinically applicable. The process began with an evidence review (available at http://stacks.cdc.gov/view/cdc/12164/) and GRADE rating of all of the data relevant to the ten key questions to inform development of the guideline. Based on the reviewed evidence, the PHS guideline was updated with the following key features:

- The guidelines clarified the optimal screening of donors, taking into account contemporary molecular assays and fourth generation antibody–antigen combination serologic assays. In large part, due to the long window period for HCV, the guideline recommends antibody and HCV NAT testing for HCV screening of all donors while enhanced screening for HIV with a fourth generation serologic assay or NAT for increased risk donors.
- All living potential donors should be tested for HIV, HBV, and HCV as close as possible to the date of the organ recovery operation, but at least within the 28-day time period prior to surgery.
- Greater details as to the components of the informed consent to be obtained for recipients of organs from increased risk donors, based predominately on expert opinion.
- Enhanced clarity about the need for testing of recipients post-transplant with assays that directly detect the presence of the virus (i.e., NAT or HBsAg) and greater clarity about the timing of recipient screening for inadvertent transmission of HIV, HBV, and HCV (testing for all three viruses within 3 months of donation and testing for HBV at 12 months post-transplant), based predominately on expert opinion.
- Greater details about the collection and maintenance of donor specimens for later use as part of a transmission investigation, based predominately on expert opinion.

Table 2 Residual risk of undiagnosed human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection per 10,000 donors at increased risk of infection

Risk Factor	HIV		HCV	
	Serology Alone	Serology + NAT	Serology Alone	Serology + NAT
Men who have sex with men	8.3	3.4	36.0	3.8
Nonmedical intravenous, intramuscular, or subcutaneous drug use	12.9	5.3	350.0	37.8
Hemophilia	0.05	0.02	0.46	0.05
Persons who have had sex in exchange for money or drugs	2.9	1.2	107.8	11.5
Partners with any of the above risk factors	2.7	1.1	126.2	13.5
Individuals who have been exposed to blood or blood products from someone with HIV or HCV	1.3	0.5	22.0	2.3
Incarceration	1.5	0.6	68.6	7.3

Source: [16••, 17••]. Residual risk is the rate of undetected infection depending on risk factor and testing strategy

- Updated criteria for defining donors at increased risk of transmitting HIV, HBV, and HCV, based predominately on evidence (see Table 3).
- Most importantly, the guideline outlines 20 areas where further studies are needed to provide improved evidence to refine the guideline in the future.

Overall, the revised guideline provided clearer delineation of which donors were at increased risk compared to the 1994 guideline, removed several criteria, and narrowed the risk period from 5 to 1 year generally; only one new criterion was added. The revised criteria in the current PHS guidelines should have resulted in slightly lower to stable numbers of donors categorized as increased risk with the new guidelines [25]. In actual practice, though, there has been a significant increase in the number of donors labeled as increased risk under the revised PHS guidelines. In the first period analyzed after implementation of the revised criteria, 19.5 % donors were labeled increased risk donor, compared to 10.4, 12.2, and 12.3 % in the three most recent years under the old guidelines (IRR = 1.45, $p < 0.001$), with increases in 44 of the 59 OPOs [26]. For reasons that are somewhat unclear, African-Americans were 52 % more likely to be labeled increased risk with the revised guidelines in place (RR = 1.52, $p = 0.01$). Clearly, this is an unintended consequence of the revision which reduces the utility of the tool. With an increased percentage of the donor pool being labeled as increased risk, it makes it harder for clinicians and patients to fully recognize the highest risk donors that represent the highest residual risk of undiagnosed infections.

Table 3 2013 US PHS guideline increased risk donor criteria

Donors at increased risk of HIV, HBV, or HCV

- People who have had sex with a person known or suspected to have HIV, HBV, or HCV infection in the preceding 12 months
- Men who have had sex with men (MSM) in the preceding 12 months
- Women who have had sex with a man with a history of MSM behavior in the preceding 12 months
- People who have had sex in exchange for money or drugs in the preceding 12 months
- People who have had sex with a person who had sex in exchange for money or drugs in the preceding 12 months
- People who have had sex with a person who injected drugs by intravenous, intramuscular, or subcutaneous routes for nonmedical reason in the preceding 12 months
- A child who is ≤18 months of age and born to a mother known to be infected with or at increased risk for HIV, HBV, or HCV infection
- A child who has been breastfed within the preceding 12 months and the mother is known to be infected with or at increased risk for HIV, HBV, or HCV infection
- People who have injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reason in the preceding 12 months
- People who have been in lockup, jail, prison, or a juvenile correction facility for more than 72 consecutive hours in the preceding 12 months
- People who have been newly diagnosed with or have been treated for syphilis, gonorrhea, *Chlamydia*, or genital ulcers in the preceding 12 months

Donors at increased risk of HCV only

- People who have been on hemodialysis in the preceding 12 months

Source: [23•, 24]. With permission from [24]

As a result of this disturbing trend, there is the need to rapidly collect more information to inform an optimized definition of increased risk donors. Key to collecting this information is more routine collection of data to inform which patients are most likely to have an undiagnosed infection that can be transmitted to the recipients. This will require that centers become more compliant with recipient screening to allow for the recognition of all transmitted infections. From the reports of donor-derived disease transmissions, centers cannot rely on serologic testing of recipients post-transplant alone. In every reported donor-derived transmission of HCV since the advent of DTAC, the serology has been negative in the recipients despite relative high viral loads, irrespective of the time since transplant [18, 27•, 28•, 29, 30]. In many of the transmission events, negative HCV recipient serology led to a delay in recognition of transmission of hepatitis.

More data are needed to identify the highest risk patients in the context of changing epidemiology and donor screening. Even with the use of sensitive NAT assays, there is a residual risk of disease transmission, as demonstrated in three recently reported transmissions [30]. This case series highlights that the residual risk of an undiagnosed infection is greatest in donors at highest risk for incident infections: active nonmedical injection drug users. Further, the residual risk remains higher when the donor screening is performed within the test window period. As such, consideration should be given to a more nuanced risk stratification system of labeling those donors as at increased risk of disease transmission. With a more nuanced risk stratification, attention can be focused on those most likely to have an infection that is not detected through routine donor screening. Further, with the recent OPTN requirement that all organ donors be screened by standard serology in addition to HCV NAT, the capacity of routine NAT will expand at all OPOs and the most sensitive tests will be applied to all donors, irrespective of risk.

Further, these cases raise the question of the role of fourth generation antibody–antigen combination assays for donor screening, which have been recommended by the current guideline as an alternative to HIV NAT in screening of increased risk donors. While these assays are less technically complex than NAT, they have a longer window period when compared to NAT. The HIV antibody–antigen can only detect infection 7–16 days after acquisition compared to HIV NAT, which can detect infection 5–6 days after acquisition [31]. Having the narrowest window seems essential especially since

donor testing is frequently done within only a few days following admission to the hospital and therefore potentially within the window period for the available tests.

Conclusion

In summary, the US PHS has developed and refined guidelines that allow the identification of donors at increased risk of transmission of HIV, HBV, and HCV [8••, 23•]. The current guidelines are far from perfect and need to continue to be revised based on changing epidemiology of infections in the donor population, changing screening technology and capacity, and lessons gained through assessment of disease transmission events. Further, the current guideline outlines a number of critical research questions that must be answered to inform a more precise definition of the highest risk donors. Unfortunately, funding to conduct such research remains mostly elusive. As such, the transplant community needs to learn from the blood community and develop some of the data through collection of already available but currently uncollected data. Most importantly, the transplant community needs to rethink the current dichotomous risk nomenclature as it related to donors at increased risk of disease transmission. A more nuanced, linear model of risk has been developed but it needs to be optimized to make the data more easily understandable to clinicians and patients [32]. Only with a more nuanced risk stratification will it be possibly to truly identify donors at highest risk of disease transmission and to allow the patients to truly make an informed decision as to whether to accept the organs or not. Lastly, transmission of HIV, HBV, and HCV through organ transplantation remains an incredibly rare event. Future robust risk stratification schema need to take into account the wide range of diseases that can be inadvertently transmitted from donor to recipient and expand the classification beyond just HIV, HBV, and HCV.

Compliance with Ethics Standards

Conflict of Interest Michael G. Ison has received research support, paid to Northwestern University, from Alios, Anolinx, Astellas, Beckman Coulter, Chimerix, Gilead, Jansen/Johnson & Johnson, and Vertez/Johnson & Johnson. He has provided compensated consultation to Biota, Celltrion, Chimerix, Farmark, Genentech/Roche, and Shionogi, and uncompensated consultation to Adamas, BioCryst, Biota, Cellex, Clarassance, GlaxoSmithKlein, GenMarkDx, Romark, Toyama/MediVector, NexBio, Theraclone, and Vertex. He is also a paid member of data and safety monitor boards related to research activity conducted by Astellas and Jansen/Vertex.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of Particular Interest, Published Recently, Have Been Highlighted as:
- • Of Importance
- •• Of Major Importance

1.• Centers for Disease Control and Prevention. Prevention of acquired immune deficiency syndrome (AIDS): report of inter-agency recommendations. MMWR Morb Mortal Wkly Rep. 1983;32(8):101–3. **This is the initial guideline from the US Interagency Working Group on AIDS to prevent transmission, including through organ donation**.

2. Centers for Disease Control and Prevention. Provisional public health service inter-agency recommendations for screening donated blood and plasma for antibody to the virus causing acquired immunodeficiency syndrome. MMWR Morb Mortal Wkly Rep. 1985;34(1):1–5.

3. Centers for Disease Control and Prevention. Testing donors of organs, tissues, and semen for antibody to human T-lymphotropic virus type III/lymphadenopathy-associated virus. MMWR Morb Mortal Wkly Rep. 1985;34(20):294.

4. Centers for Disease Control and Prevention. Human immunodeficiency virus infection transmitted from an organ donor screened for HIV antibody–North Carolina. MMWR Morb Mortal Wkly Rep. 1987;36(20):306–8.

5. Quarto M, Germinario C, Fontana A, Barbuti S. HIV transmission through kidney transplantation from a living related donor. N Engl J Med. 1989;320(26):1754.

6. Samuel D, Castaing D, Adam R, et al. Fatal acute HIV infection with aplastic anaemia, transmitted by liver graft. Lancet. 1988;1(8596):1221–2.

7.•• Simonds RJ, Holmberg SD, Hurwitz RL, et al. Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor. N Engl J Med. 1992;326(11):726–32. **This is the first major report of HIV transmission through organ and tissue donation after the use of serologic screening of donors**.

8.•• Centers for Disease Control and Prevention. Guidelines for preventing transmission of human immunodeficiency virus through transplantation of human tissue and organs. MMWR Recomm Rep. 1994;43(RR-8):1–17. **This is the US CDC guideline that formed the based of the original OPTN definition of donors at increased risk of disease transmission**.

9. Chappel RJ, Wilson KM, Dax EM. Immunoassays for the diagnosis of HIV: meeting future needs by enhancing the quality of testing. Future Microbiol. 2009;4(8):963–82.

10. Centers for Disease Control and Prevention (CDC). Clarification of human immunodeficiency virus screening practices for organ donors. Washington: Federal Register; 1996. p. 56458–9.

11.• Ison MG, Stosor V. Transplantation of high-risk donor organs: a survey of US solid organ transplant center practices as reported by transplant infectious diseases physicians. Clin Transpl. 2009;23(6):866–73. **This provides data on the state of transplant center practices related to increased risk donors in the United States at the time of the HIV-HCV co-transmission event**.

12.•• Ison MG, Llata E, Conover CS, et al. Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients. Am J Transplant. 2011;11(6):1218–25. **This is the definitive report of the investigation of the co-transmission of HIV and HCV from an organ donor to four recipients in the United States**.

13. Gordon EJ, Ison MG. Decision aids for organ transplant candidates. Liver Transpl. 2014;20(7):753–5.

14. Gordon EJ, Reddy E, Ladner DP, Friedewald J, Abecassis MM, Ison MG. Kidney transplant candidates' understanding of increased risk donor kidneys: a qualitative study. Clin Transpl. 2012;26(2): 359–68.
15. Gordon EJ, Beauvais N, Theodoropoulos N, et al. The challenge of informed consent for increased risk living donation and transplantation. Am J Transplant. 2011;11(12):2569–74.
16.•• Kucirka LM, Sarathy H, Govindan P, et al. Risk of window period hepatitis-C infection in high infectious risk donors: systematic review and meta-analysis. Am J Transplant. 2011;11(6):1188–200. **This is a meta-anlysis of all data to estimate the risk of disease transmission after serology or serology plus NAT screening of organ donors for HCV**.
17.•• Kucirka LM, Sarathy H, Govindan P, et al. Risk of window period HIV infection in high infectious risk donors: systematic review and meta-analysis. Am J Transplant. 2011;11(6):1176–87. **This is a meta-anlysis of all data to estimate the risk of disease transmission after serology or serology plus NAT screening of organ donors for HIV**.
18. Centers for Disease Control and Prevention. Potential transmission of viral hepatitis through use of stored blood vessels as conduits in organ transplantation–Pennsylvania, 2009. MMWR Morb Mortal Wkly Rep. 2011;60(6):172–4.
19. Marelli D, Bresson J, Laks H, et al. Hepatitis C-positive donors in heart transplantation. Am J Transplant. 2002;2(5):443–7.
20. Pereira BJ, Milford EL, Kirkman RL, Levey AS. Transmission of hepatitis C virus by organ transplantation. N Engl J Med. 1991;325(7):454–60.
21. Pereira BJ, Wright TL, Schmid CH, Levey AS. A controlled study of hepatitis C transmission by organ transplantation. The New England organ bank hepatitis C study group. Lancet. 1995;345(8948):484–7.
22.• Centers for Disease Control and Prevention. HIV transmitted from a living organ donor–New York City, 2009. MMWR Morb Mortal Wkly Rep. 2011;60(10):297–301. **This is the report of HIV transmission through living kidney donation**.
23.• Seem DL, Lee I, Umscheid CA, Kuehnert MJ, United States Public Health S. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. Public Health Rep. 2013;128(4):247–343. **In this paper, the authors present the detail report of the US Public Health Services Guidelines on preventing transmission of HIV, HBV and HCV through organ transplantion, including details supporting evidence**.
24. Seem DL, Lee I, Umscheid CA, Kuehnert MJ. Excerpt from PHS guideline for reducing HIV, HBV and HCV transmission through organ transplantation. Am J Transplant. 2013;13(8):1953–62.
25. Ison MG, Schultz EM, Jendrisak MD. Impact of proposed US public health services guidelines for increased risk organ donors: a single OPO analysis. In: American transplant congress. (Ed.^(Eds) Seattle, Washington: 2013.
26. Kucirka LM, Bowring MG, Massie AB, Luo X, Nicholas LH, Segev DL. Landscape of deceased donors labeled increased risk for disease transmission under new guidelines. Am J Transplant. 2015.
27.• Green M, Covington S, Taranto S, et al. Donor-derived transmission events in 2013: a report of the organ procurement transplant network Ad Hoc disease transmission advisory committee. Transplantation. 2015;99(2):282–7. **This was the provides an update of the OPTN/UNOS Disease Transmission Advisory Committee's data on the epidemiology of donor-derived infections through transplantation in the US**.
28.• Ison MG, Hager J, Blumberg E, et al. Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS disease transmission advisory committee. Am J Transplant. 2009;9(8):1929–35. **This was the initial report of the OPTN/UNOS Disease Transmission Advisory Committee which provides the initial epidemiology of donor-derived infections through transplantation in the US**.
29. Ison MG, Nalesnik MA. An update on donor-derived disease transmission in organ transplantation. Am J Transplant. 2011;11(6): 1123–30.
30. Suryaprasad A, Basavaraju SV, Hocevar SN, et al. Transmission of hepatitis C virus from organ donors despite nucleic acid test screening. Am J Transplant. 2015;15(7):1827–35.
31. Perry KR, Ramskill S, Eglin RP, Barbara JA, Parry JV. Improvement in the performance of HIV screening kits. Transfus Med. 2008;18(4):228–40.
32. Chow EK, Massie AB, Muzaale AD, et al. Identifying appropriate recipients for CDC infectious risk donor kidneys. Am J Transplant. 2013;13(5):1227–34.