OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC)
Meeting Summary
February 14, 2022
Conference Call – Open Session

Ricardo La Hoz, MD, FACP, FAST, Chair
Lara Danziger-Isakov, MD, MPH, Vice-Chair

Introduction

The Ad Hoc Disease Transmission Advisory Committee (DTAC) met via Citrix GoToMeeting teleconference on 02/14/2022 to discuss the following agenda items:

1. *Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing* Public Comment Proposal Update
2. Living Donor Committee Public Comment Proposal: *Modify Living Donor Exclusion Criteria*
3. Endemic Workgroup Update & Next Steps

The following is a summary of the Committee's discussions.

1. *Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing* Public Comment Proposal Update

The DTAC Vice Chair updated the committee on the proposal currently out for public comment to update *Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing.* This proposal has been generally supported, and there have been a few comments discussing using a weight threshold for testing instead of an age threshold. The Vice Chair also mentioned that the workgroup had discussed the potential for a weight threshold, and discussed it with the CDC, before deciding to use an age threshold. She also mentioned that the DTAC had sent a statement that the Executive Committee had approved, in support of the revision to the PHS Guideline currently out in the Federal Register, which would allow this proposal to occur.

A CDC representative mentioned that once the federal public comment period closes, the CDC will be drafting a policy update in the MMWR to print for June or July 2022.

A UNOS staff member also highlighted the six comments from community members asking the committee to consider weight instead of age for criteria, and that while the workgroup did consider this the committee should be aware that these comments have occurred and consider whether any changes may be needed after public comment. She also highlighted that the workgroup had been more concerned about adolescent behavior being associated with potential risk.

2. Living Donor Committee Public Comment Proposal: *Modify Living Donor Exclusion Criteria*

The OPTN Living Donor Committee Vice Chair presented on his committee's proposal to *Modify Living Donor Exclusion Criteria* currently available for public comment. The purpose of this proposal is to ensure the relevancy of living donor exclusion criteria, propose modifications supported by current research, broaden individuals' opportunities to become living organ donors, all while maintaining living donor and transplant recipient safety. Proposed modifications relevant to DTAC include a modification from exclusion criteria from "active malignancy, or incompletely treated malignancy" to "active or incompletely treated malignancy that requires treatment, other than surveillance, or more than minimal

risk of transmission". The rationale for this change is that current guidelines and literature show that individuals with low-grade malignancies, where there is minimal risk of transmission, may be acceptable and safe as living donors. The Living Donor Committee had reviewed a previous DTAC publication on transplant-transmitted malignancies and the general risks of transmission for different malignancy types when developing this recommendation. Another rationale for this change is that consideration of these potential living donors should be individualized and based on clinical judgment and comprehensive informed consent. Discussion questions included whether the committee agreed with the exclusion criteria modifications, and if the malignancy exclusion criterion was clear and how a transplant program would interpret minimal risk of transmission.

DTAC members thanked the Living Donor Vice Chair for presenting and stated that the proposal strikes a great balance between donor/recipient safety and increasing the potential donor pool. They also felt it was important to ensure that malignancy risk evaluation include both risk of transmission to the recipient as well as risk of the donor requiring longer term treatment that may be affected by organ donation. The Living Donor Vice Chair mentioned that there isn't currently data on how organ donation may impact future malignancy treatment, but that the goal of the Living Donor Committee is to enhance living donation while protecting donor and recipient safety, and that they did discuss this point.

The Chair asked the DTAC and the Living Donor Vice Chair if it would be helpful to update the previous DTAC publication on transplant-transmitted malignancies, since it has been 11 years since original publication and a significant amount of data has accrued. A pathologist committee member on the call mentioned that he would be happy to work on the update, and multiple committee members and the Living Donor Vice Chair agreed that this would be helpful to the community as a whole when assessing risk of malignancy transmission. The Living Donor Vice Chair also mentioned that if the DTAC were able to assess any data on living donor outcomes from malignancy treatment post-donation and the impact of having a single kidney or having donated a liver it would be incredibly helpful information.

3. Endemic Workgroup Update & Next Steps

The DTAC Chair updated the committee on the recent work of the Endemic Diseases Workgroup. The review of the project includes reviewing potential gaps in education, policy, or data related to certain endemic diseases with significant patient safety risks, with an initial focus on Tuberculosis (TB), Strongyloides, Trypanosoma cruzi (Chagas), and West Nile Virus (WNV). These diseases have high potential for complications and potential mortality if transmitted to recipients, but many are easily preventable or treatable with prophylaxis if detected early. The committee has previously expressed concerns that an increase in travel for organ transplant needs to include an increase in awareness of and communications for potential endemic diseases that may differ between regions. Challenges to addressing the problem include a lack of available data to describe the extent of the risk, as well as variation in pathogen-specific screening tests, OPO screening practices, and regional and/or seasonal prevalence. Leadership has presented these concerns to the Transplant Administrators, Transplant Coordinators, and OPO committees, who have all agreed that this is a problem. The Transplant Coordinators Committee emphasized that there is inconsistency between OPOs for screening and assessment of risk factors, and the data for these is not easily identifiable in UNet. The OPO Committee was not opposed to testing but emphasized that the timing of the testing is important, and that the committee has to be mindful of when the tests will be required to be available. They wanted to ensure that there is proper assessment of feasibility of testing, including when post-recovery results would be okay. They had also expressed concerns that there are places for some testing in in UNet, but not fields to record risk factors and not fields for all testing results. In addition, the committee had received a memo from the Membership and Professional Standards Committee (MPSC) stating that "existing policies [are] not being followed… [with a] wide variation in practice" and that "timing of reports varies".

A CDC member asked if there was an existing policy for testing. The Chair and UNOS staff clarified that there isn't existing policy, just guidance documents.

A CDC member stated that he thought that WNV and TB should be prioritized He said that there is existing blood donor screening for WNV, with routine high throughput testing for other products of human origin, and that the testing is very sensitive and specific. In addition, he pointed out that there are clear patterns of seasonality and geography of disease for WNV, and it's demonstrated as transplant transmissible with some evidence of organ reservoirs for WNV. He also mentioned that he had already spoken with a subject matter expert in the CDC Division of Vector Borne Diseases who would be able to do a presentation on seasonality, geography, and testing for WNV to help inform the workgroup discussions. The Chair asked committee members if they had any thoughts on when WNV testing should be available. One Committee member stated that he had been performing WNV testing at two separate OPO labs for at least five years on every organ and tissue donor, and that the testing is easy to perform but that he hasn't had a single positive in five years. He also stated that he had two cases being investigated for potential WNV transmission to recipients, and that the existing Nucleic Acid Test (NAT) platform gave negative results. He also mentioned that WNV is only viremic for a short time, with literature to support that, which might limit the clinical utility of the assay to effectively detect the presence of virus. The Committee Chair mentioned that his local OPO had a very different experience, due to their location, and that positive vs. negative results might be more of a factor of pre-test probability. A CDC representative mentioned that for blood donors, pooled testing occurs year-round and once there's a threshold of positivity, typically in the endemic season, there's individual-level testing that occurs. He mentioned that this is how he'd envision testing occurring for organ donation as well. He would think if there is evidence of active WNV activity in the donor's area of residence, that would be the indication to do testing.

The Committee Vice Chair mentioned that WNV testing may impact organ acceptance, since there isn't specific post-transplant prophylaxis for WNV. Another member agreed. The CDC representative stated that he didn't think it would make sense to do testing for every donor year-round, but since WNV has a high lethality, there aren't available therapeutics, and the testing has a quick turnaround time, the testing should be done and available at time of procurement. The Chair asked members if it would be reasonable to require WNV testing based on time of the year, seasonality, and regionality. A lab member said that the testing is reasonable, and he's been performing it at his labs for years, but he's concerned about the sensitivity due to the short viremic period. In addition, he stated that it would be more operationally difficult to implement testing based on dates or local conditions, and that it's operationally more reasonable to have less customization. A UNOS staff member also clarified that caveats for behavior that may vary based on time and place may be more appropriate for guidance than policy. The Chair mentioned that may be something for the workgroup to discuss, and that the big picture for the committee today was to prioritize the approach and then the more granular discussions can happen within the workgroup.

A CDC representative spoke up and said that tuberculosis (TB) was one of his larger concerns and has been for years. He expressed concern about the morbidity in recipients and the risk of unidentified disseminated TB, especially since next of kin interviews to assess donor risk are inherently limited. He recommended that the DTAC create standardized screening policies so that all recipients receive the same standard of care. He expressed that there would be a challenge in the recognition of latent TB, and that the type of testing that needs to be implemented is less clear. He also mentioned that TB isn't a contraindication for transplant, and that you can even recognize the TB post-transplant and still have time to mitigate risk to recipients.

The Chair replied, stating that identifying risk factors in the donor is incredibly helpful, as would be any testing that could help mitigate the risk of disease transmission. He also stated that the committee would need to work concurrently on education on acceptance of donors with risk factors of TB or evidence of disease/latent TB so that the organs are not discarded. He also mentioned that with adequate prophylaxis, even lungs can often be utilized, but the possible barriers are in identifying risk factors and what testing to implement.

Multiple members stated that there are some inherent limitations, especially with historical details often being imperfect, but that with additional information the recipients of these organs could be better managed. One member also expressed concern about acid fast bacilli (AFB) testing in lower respiratory samples, since there's often a very long turnaround time. One member stated that it may be useful in a directed manner if there are clear infiltrates on the lungs, but not all personnel will be able to do it, and it may only have true value if implemented in a specific way in specific cases. One member posed that in TB patients, in highly endemic areas, sputum cultures are used with high sensitivity and specificity, and that lavage of infiltrates may not be necessary to diagnose disease. The CDC representative replied that the CDC can present to the endemic workgroup, with data on test performance and characteristics by test, as well as if there could be an algorithm of testing that could be practically implemented and enhance recipient safety.

One member brought up a concern that prophylaxis for TB on suspicion of disease, rather than confirmed disease, could be difficult as the medications are not innocuous and often require alteration of immunosuppression due to drug interactions.

Multiple members expressed support for implementation of widespread strongyloides testing, especially due the availability and high tolerance for prophylaxis. In addition, members mentioned that the test results would not need to be available at the time of recovery or transplant, but would ideally be returned within 72 hours of transplant for recipient prophylaxis if needed. Multiple members also mentioned that there has been a significant shift in strongyloides cases reviewed over the past few years, with most cases becoming "intervention without disease transmission" (IWDT) as OPOs have increased donor testing.

Members discussed Chagas screening, and a heart physician mentioned that they are still comfortable accepting donors with risk of Chagas or positive testing, and that the treatments can be effective and safe. She mentioned that their program has extensive post-transplant testing for recipients for Chagas if the donor had risk factors. Another member mentioned there have been publications from a group in New York who has had similar experiences, with good post-transplant outcomes for heart recipients from donors positive for Chagas.

Staff confirmed that there was still broad interest in pursuing the four diseases in parallel. The Chair confirmed that the goal of the proposed committee project would be to increase the awareness of risk factors for endemic diseases, increase testing where available, and increase communication between OPOs and transplant teams to implement recipient interventions to mitigate disease transmission.

Upcoming Meetings

- March 1, 2022, 3 pm ET (teleconference; open session)
- March 28, 2022, 12 pm ET (teleconference)

Attendance

- **Committee Members**
  - Debbie Levine
  - Dong Lee
  - Gary Marklin
  - Gerald Berry
  - Jason Goldman
  - Kelly Dunn
  - Lara Danziger-Isakov
  - Michelle Kittleson
  - Ricardo La Hoz
  - Sam Ho
  - Stephanie Pouch
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **UNOS Staff**
  - Anne McPherson
  - Cole Fox
  - Courtney Jett
  - Leah Slife
  - Lindsay Larkin
  - Meghan McDermott
  - Sandy Bartal
  - Susan Tlusty
- **FDA Staff**
  - Brychan Clark
- **CDC Staff**
  - Ian Kracalik
  - Pallavi Annambhotla
  - Rebecca Free
  - Sridhar Basavaraju
- **Invited Presenters**
  - Nahel Elias