

OPTN Ad Hoc Disease Transmission Advisory Committee

Meeting Summary

September 19, 2022

O'Hare Hilton, Chicago, Illinois, Paris Ballroom

Lara Danziger-Isakov, MD, MPH, Chair

Stephanie Pouch, MD, MS, Vice Chair

Introduction

The Ad Hoc Disease Transmission Advisory Committee met in Chicago, Illinois on 09/19/2022 to discuss the following agenda items:

1. Introductions, Coffee, and Breakfast
2. Endemic Diseases: Chagas Presentation and Discussion
3. Endemic Diseases: Strongyloides Presentation and Discussion
4. Update Data Collection for Lung Mortality Models
5. HIV Positive vs. Infected project
 - a. Background/Purpose
 - b. HOPE in Action Presentation
 - c. Existing Algorithms
 - d. Medical/ Social history Considerations
 - e. Confirmatory Testing Considerations
6. Closed Session case Review
7. Case Review Efficiencies/Improvements
8. Meeting Adjourns

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

1. Introductions, Coffee, and Breakfast

Committee members and UNOS staff introduced themselves and shared how they were first introduced to transplant.

2. Endemic Diseases: Chagas Presentation and Discussion

The Past Chair presented on the Endemic Diseases Workgroup's discussion on *T. cruzi*. The goals of the discussion were to determine which deceased donors should require screening, what types of testing should be done, timing of the test results, and the creation of education material on the subject.

The Past Chair noted that vector borne transmission only occurs in the Americas, and there are currently an estimated 8 million people infected with *T. cruzi*. It is estimated that 300,000 of these people live in the U.S. and there is a mortality of up to 75%. He discussed serologic testing for *T. cruzi* and stated that ELISA and IFA tests produce the greatest accuracy. He explained that the American Society of Transplantation suggests that all organ procurement organizations (OPOs) use a targeted screening approach for *T. cruzi*. The Past Chair discussed the pre-test probability and sensitivity of these tests. The *T. Cruzi* ELIA test has a sensitivity of 94.45% and a specificity of 99.4%.

The Past Chair suggested that donors born in endemic areas should be screened. If positive, these donors should have confirmatory testing done by the CDC, but these results would not need to be back

pre-recovery. Additionally, he suggested education materials be provided to OPOs and transplant hospitals on risk factors, available screening tests, confirmatory testing, *T. cruzi* positive donor organ allocation, and transmission documentation.

Summary of Discussion

The Past Chair presented the proposed criteria for targeted *T. cruzi* screening of the donor being born in Latin America (south America, Central America, or Mexico). The Chair requested feedback from the committee on the proposed criteria and noted that there are already OPO's that do this in areas that have a higher prevalence of people born outside of the United States in their populations. A member noted that a major challenge they face is getting the test results back before going to the operating room and that travel history is also included in their screening criteria. The Chair asked if information was available about including travel or residence history as criteria. The Past Chair stated that these other criteria can be included but that place of birth was chosen for reasons of complexity and reliability of information. The Chair observed that this might increase the risk of false positives because of lower pre-test probability which the Past Chair endorsed. A member suggested an added distinction that does not include Latin American and Caribbean Islands. Another member said that from the point of view of the HLA lab, Chagas testing reliability and cost has been a significant issue, and there is concern about the ability to deal with higher testing numbers and the effect that might have in increased false positives and false negatives.

A member asked what the next steps would be for the coordinators after a donor meets this criterion. Another member said that using these criteria has not been much of an operational issue for their OPO. It was then brought up by another member that if this proposal is moved forward then there would need to be discussion about standardizing confirmatory testing. A member asked how toxic the treatment medication is and the Past Chair confirmed that the medications do have significant adverse effects. The Past Chair explained the workflow: if the donor screens positive then submit confirmatory testing, if the donor is confirmed positive then the recipient needs to be monitored by PCR (CDC has published guidelines), and if the recipient tests positive then they are administered treatment for eight weeks.

Several members reiterated concerns about testing performance and timing and the Past Chair emphasized the importance of doing the testing. A member from CDC noted that currently CDC is acting as the confirmatory lab and the primary place performing PCR monitoring post-transplant and acknowledged the challenges regarding confirmation of chagas disease and the timing in terms of donor derived infection. The member said that confirmatory testing takes several days. The Chair asked the committee whether having universal targeted screening helps improve the safety of potential recipients and if it is at the cost of potentially losing some cardiac donors. A member from the CDC did confirm that there are recipients who acquired donor derived chagas from at risk donors that were not screened but did not know how screening would impact heart transplants.

The Chair decided to skip the second question about what testing to use as the member from the CDC already outlined the testing that is available that they perform.

The Past Chair posed the third question: when do the results need to be back by, pre-recovery given the risks to the heart recipient, or post-recovery? The Chair clarified that this would be regarding only the screen testing, and not the confirmatory testing.

The Past Chair presented the final point of the discussion on creating education materials for OPO's and transplant hospitals regarding *T. cruzi* risk factors, testing, and transplant considerations. A member stated that it seems this issue will continue to become more prevalent due to continued immigration, and the Chair added that this could be important for OPO's and transplant centers in areas of the

country that have not had much experience with Chagas yet. A member asked if the inclusion of criteria for donors whose mother was Chagas positive was because of vertical transmission. The past chair confirmed that is correct and vertical transmission of Chagas in endemic areas is quite common.

The committee agreed to move forward with action related to Chagas screening. A member agreed with going with the suggestion of the Past Chair to screen for place of birth and noted that travel history may be less reliably gathered. The Chair noted that this recommendation would be a minimum requirement but OPO's can screen more if that was warranted, and the committee needs to balance any increased burden on the OPO's. A member said that from the OPO perspective, adding the Chagas testing on to the lab request is relatively easy. A member added that from the laboratory perspective there are some challenges and suggested that the proposed criteria begin as guidance instead of a policy requirement so that OPO's and Labs can get up to speed. The Past Chair confirmed that for the nine donors who died between 2002 and 2009 there was no screening in place but believes that number is underreported. In terms of screening results and timing, the Past Chair said that it is not recommended to transplant a heart from a Chagas positive donor, but that for other organ recipients' penetrance varies but results are good. The Past Chair also reported that after discussion with other committees about the project, there were concerns raised about continued lack of screening even if the donor meets criteria unless it is made into a policy. A member brought up that if the screening criteria were to be more stringent and only include the top 5 or so countries that Chagas is most endemic in, it would limit the increased administrative and testing burden as well as the possibility of false positives.

Next Steps:

The Chair concluded that the consensus of the committee seemed to be to move forward with making this into policy and will take it to OPTN Executive Committee for review.

3. Endemic Diseases: Strongyloides Presentation and Discussion

The Chair introduced the presentation on Strongyloidiasis epidemiology and donor derived cases given by CDC Staff.

CDC Staff stated that there is an estimated 370-600 million people infected worldwide. She stated risk factors include lack of effective sanitation, skin (bare feet), and contact with contaminated soil. She noted there is an undefined risk associated with short duration travel. In the U.S., there is limited evidence of locally acquired infections.

Summary of Discussion:

The Chair opened the discussion with the next steps for the committee to decide on: what screening criteria to use, should this be guidance or policy, and what education materials would be needed. The Chair began by addressing the question of test result timing by saying that most results come back after recovery, there is a high rate of intervention with therapy without transmission, and the therapy used is benign. The Chair asked the committee if they agreed with not needing results prior to recovery and there was a consensus for yes.

The next question the Chair posed to the committee was regarding who should be screened; whether it should be universal screening or targeted screening. A member mentioned that for his OPO testing is done for every organ donor if an organ was utilized in transplant. The Past Chair noted that targeted screening criteria could be difficult to obtain accurately. Another member noted that with a test that is relatively available and accurate and a treatment that is benign, trying to add complexity through targeted screening does not make much sense. Another member noted their support for expanded criteria. The Chair noted that a recent study reported that 23.9% of OPO's were screening for this disease. A member said that targeted screening would be very difficult with this disease and was in favor of

screening all donors and another member was in support of this as well. Another member noted that screening is made easier because even if there is a positive result, the organs can still be utilized and there does not seem to be much downside. The Chair confirmed that the consensus is to move forward with a universal screening policy that does not need to be resulted prior to recovery and with the inclusion of educational materials.

Next Steps:

The Committee agreed on universal screening for all donors and that this would be put into policy.

4. Update Data Collection for Lung Mortality Models

The Vice Chair presented a current proposal regarding expanding data collection on disease severity of lung candidates.

The Committee discussed the following data collection on microbiology:

Microbiology: If the patient has a history of infection (either within the last year or one year ago) with a multi- drug resistant organism select the type of organism. If the history of infection is not listed below, it does not need to be reported.

- Burkholderia cenocepacia
- Burkholderia gladioli
- MDR or Pan-R gram negative bacteria
- Mycobacterium abscessus
- Scedosporium/Pseudallescheria species complex

Summary of Discussion:

The Vice Chair requested feedback on the proposed changes and if there were any suggested infectious diseases or malignancies that should be added to the proposal. A member requested a definition for MDR or Pan-R gram negative bacteria and the Vice Chair said that was something that needs to be followed up on to see if any of the definitions offered by the committee in December were utilized. A member asked for clarification as to how the organisms for the added criteria were chosen and the Vice Chair said that they were chosen by the lung committee based on previously published data related to post transplant outcomes. Operational considerations and the Cystic Fibrosis Foundation data were also factored in when making that decision. A member suggested that given the operational considerations would it make more sense to make the list less specific and group some of the organisms together. A member stated that it is still important to consider that all the listed pathogens have been documented in the literature to have impacted transplant outcomes. The Chair noted that so far there has been a proposal to ensure the definition that is being used by the Lung Committee is either the one supplied by the DTAC or one that is outlined in literature. A member asked if the results are based on colonization versus active infection and the Vice Chair responded that there is not necessarily a delineation between the two. Another member mentioned that risk factors for immunodeficiency might also be important factors to gather data on. A member said that the proposed list seems mostly focus on Cystic Fibrosis related factors and thinks that Interstitial Lung Disease related factors should be considered as well.

The Chair called a break for the committee.

5. HIV Positive vs. Infected Project

The Chair presented on the committee project to develop an algorithm for OPTN policy related to designating HIV infected status based on available testing. This is to ensure that HIV infected organs are

not transplanted into HIV uninfected recipients and to reduce underutilization of organs by ensuring they are allocated with the correct infectious disease status.

The Chair explained that clinical situations have arisen where some deceased donors with at least one positive HIV test were treated as if not infected with HIV and allocated to candidates not infected with HIV. OPTN Policy references use terminology “HIV positive” donors (versus HIV infected donors). Historically, any positive result has been treated as HIV positive and thus subject to HOPE Act policies (HIV+ to HIV+ allocation/transplantation)/ OPTN Policy has not attempted to account for HIV positive test results for HIV uninfected donors, however recent events have raised the question and the need for further clarification.

The Committee discussed:

- What (if any) testing results could be used to classify a deceased donor as not infected with HIV although the donor has at least one positive HIV test result?
- What (if any) clinical judgment or individual protocols would be appropriate and consistent with requirements to assess suspected HIV uninfected donors with HIV positive test results?

A John Hopkins employee presented to the Committee on the rate of HIV positive tests for HIV uninfected donors. She presented an algorithm to the committee that would help differentiate from HIV positive and HIV infected in donors.

Summary of Discussion:

The Chair requested feedback on utilizing the 2020 PHS Bloodborne Pathogen Risk Criteria in the creation of this algorithm and if those criteria should be an automatic rule out for being able to label a donor as HIV uninfected. The Chair clarified that the terminology of “true positive” and “false positive” cannot be used in this context and instead the purpose is to sort out if there are circumstances in which a donor that tests positive on a screening test can be relabeled as HIV uninfected based on confirmatory testing. The law says that an organ cannot be transplanted from an HIV infected donor to an HIV uninfected recipient. A member stated that OPO’s are already making those interpretive decisions and the Chair responded that DTAC has been asked to provide specific guidance because those decisions are being done unevenly. Further clarifying, the Chair said that this guidance would be based on confirmatory testing prior to organ allocation because of the impact that HIV infected status has on the match run. A member asked if the testing would be available in a reasonable amount of time and wanted to keep the recipient perspective in mind considering how devastating transmission can be. A member asked for clarification if the screening test refers to the HIV antigen antibody tests and the confirmatory test refers to the HIV NAT testing and the Chair replied that it is part of what the committee needs to discuss. A member stated that all the tests used in the laboratories for the OPO’s are screening tests, and this would be making a diagnosis based on assays that are not designed to be used that way. This forces the OPO to make decisions about the donors, sometimes without the bandwidth to pursue consultations, and so defining what will be considered confirmatory testing will be important. A member reiterated that point of this guidance would be to create a minimum acceptable standard for evaluating donors for HIV. The Past Chair observed that it is important to look after the safety of the recipient but when looking at the pre-test probability slopes for the HIV antigen antibody and NAT tests, there will always be some incorrect results and a system that has no tolerance and leads to zero transmissions will lead to a fair amount of mortality on the waitlist. There is a balance that needs to be found to safely determine that the donor is uninfected, in a way that can be done by the OPO, to not lose the organs.

The question of how the NAT testing is being performed was brought up due to influence that batching samples can have on the results, and a member confirmed that is being looking into now, but the information was not currently known. Another member noted that in their experience, most of the testing done by OPO's is not done in batches and that sample contamination should be very rare.

The Chair opened discussion after the HOPE in Action presentation to determine what type of testing should be acceptable, how to integrate that with knowledge and understanding of risk behavior or medical therapies that individuals might be getting, and how to accomplish that safely. A member asked about the definition used for a donor meeting risk criteria and the presenter clarified that they did not always consider a donor as meeting criteria even if the OPO did due to utilizing more stringent criteria. A member asked if a donor was antibody negative and NAT positive on a qualitative screening test, with risk factors or an unknown history, would they be considered as potentially uninfected and who would make that determination based on the proposed algorithm. The Chair noted that is one of the decisions that the committee needs to make, and the presenter replied that if there were acute risk factors then they would probably not consider the donor potentially uninfected.

A member said that in the presented algorithm the quantitative pathway to determining infected status is harder and takes more time, while the other pathway of screening with the Western blot was quicker and asked if donors without risk factors and a positive antibody test but a negative Western blot should be considered uninfected, and organs utilized. Another member noted that there is a significant time difference between when a Western blot test and a screening test can become positive, up to 25 days, and that is why the CDC moved away from using Western blot for diagnosis. The NAT testing can be done faster and at more labs than the Western blot. A member suggested pairing the algorithm with guidance for consent considering there will be at least one positive result and this could help with moving towards a model with some risk tolerance instead of zero risk tolerance. The Past Chair asked what might happen if a new policy is implemented and there is a transmission given that the law regarding HIV transplant is a zero-tolerance policy. It was emphasized that any definition of an HIV uninfected donor needs to be based on scientifically sound data. The Chair summarized discussion and requested volunteers to continue working on this project.

Next Steps:

The Committee decided to create a workgroup that would discuss the creation of an algorithm.

6. Closed Session Case Review

The committee reviewed current disease transmission cases in a closed session.

7. Case Review Efficiencies/Improvements

The Chair presented on case review efficiencies and the recent changes that have been made for the process. The goal of the discussion was to brainstorm further changes and improvements for the case review process.

Presentation Summary:

- Previous changes:
 - Launched consent case packet process
 - Piloted aggregate case review groups (bacterial, blood borne viral, fungal, endemic diseases, and pathology)

Summary of Discussion:

The Chair began the discussion by asking if the current case groupings make sense, are the case groupings too broad, is there commonly requested data that should be gathered earlier, is there data that should be more specific, and if there is any other feedback. A member said that it could be helpful in liver cases to know the patient's MELD/PELD score as that would aid in assessment. A member noted that there seems to generally be more information gathered for the donor and having more for the recipient could be helpful. The Chair requested that someone put together a list of relevant questions to send to the recipient side that would help with this efficiency. The Past Chair stated that he thinks the case grouping system has been a significant improvement. A member suggested that for the pathology cases it could be very helpful to have a complete autopsy done on the donor to see if there was a possibility that a recipient's tumor could have come from another organ in the donor. The Chair requested feedback on the consent cases and a member noted that having some guidelines for adjudication could be helpful, especially for the first time, but otherwise the feedback was positive. A member asked about how to maintain consistency of adjudications over time and the Chair noted that is an important consideration, but they had not yet figured out best practices, partially because there have been fewer cases that have difficulties with adjudicating. The Chair recommended that group leaders bring forward difficult adjudications so that data can be collected on that. UNOS support staff asked if it would be possible to consolidate case forms at the end of a case review for submission, and multiple leaders said that they had already been consolidating to spreadsheets to help themselves keep track. The Chair recommended a template be created to facilitate this. The Past Chair noted that in the previous method, the greatest benefit that came from all committee members reviewing cases was the learning and information that was gained and could be passed on to their respective organizations. The Past Chair said that a method to capture and share those lessons with the whole committee as well as track trends that might lead to actionable changes to help the system would be valuable. A member recommended that trends be tracked in the annual report if possible.

Next Steps:

- MELD/PELD score
- Recipient questions
- Adjudication guidelines
- Case review form consolidation template

8. Meeting Adjourns

The Chair thanked everyone for coming to this in person meeting and looks forward to welcoming as many committee members as possible at the next in-person meeting.

Upcoming Meeting

October 4, 2022, 3pm EST, teleconference

Attendance

- **Committee Members**
 - Ann Woolley
 - Jason Goldman
 - Kelly Dunn
 - Lara Danziger-Isakov
 - Ricardo La Hoz
 - Anil Trindade
 - Sam Ho
 - Sarah Taimur
 - Dong Heun Lee
 - Stephanie Pouch
 - Chuck Marboe
 - Lorenzo Zaffiri
 - Helen Te
 - R. Patrick Wood
 - Cynthia Fisher
 - Marty Sellers
 - Judith Anesi
- **HRSA Representatives**
 - Jim Bowman
 - Marilyn Levi
- **CDC Staff**
 - Sridhar Basavaraju
 - Sue Montgomery
 - Ian Kracalik
 - Pallavi Annambhotla
 - Rebecca Free
- **FDA Staff**
 - Brychan Clark
- **SRTR Staff**
 - First Name Last Name
- **UNOS Staff**
 - Taylor Livelli
 - Carson Yost
 - Susan Tlusty
 - Nelson Marrero
 - Krissy Laurie
 - Lee Ann Kantos
 - Sandy Bartal
- **Other Attendees**
 - Christine Durand