

## **OPTN Ad Hoc Disease Transmission Advisory Committee**

### **Meeting Summary**

**September 28, 2021**

### **Conference Call**

**Ricardo La Hoz, MD, FACP, FAST, FIDSA, Chair**

**Lara Danziger-Isakov, MD, MPH, Vice Chair**

### **Introduction**

The Ad Hoc Disease Transmission Advisory Committee met via Citrix GoToMeeting teleconference on 09/28/2021 to discuss the following agenda items:

1. DTAC-Pediatric Workgroup Update
2. Public Comment Update
3. Public Comment Presentations
4. Require Lower Respiratory Testing for SARS-CoV-2 Monitoring Report
5. Geographically Impacted Diseases
6. Closed Session Medical Peer Review

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

#### **1. DTAC-Pediatric Workgroup Update**

DTAC Vice Chair presented on the discussions of the DTAC-Pediatric Workgroup formed to discuss pediatric requirements for candidate pre-transplant HIV, HBV, and HCV testing.

##### Data summary:

The CDC presented an abridged data report on the incidence of HIV, HBV, and HCV in children in the United States and safe blood volumes for draw on healthy children. The full presentation was given to the DTAC-Pediatric workgroup on July 30<sup>th</sup>.<sup>1</sup>

The DTAC Vice Chair stated that given the data, the workgroup is amending the OPTN policy requirements for children to have HIV, HBV, and HCV testing in the hospital admission. The Vice Chair mentioned that the workgroup is still finalizing the details of the change, including age ranges and testing timeframes, but that there would still be a testing requirement at some point in the transplant evaluation.

##### Summary of discussion:

A CDC representative mentioned that the CDC is planning to update the PHS Guideline to address this issue to ensure that OPTN policies remain consistent. A member of the DTAC expressed appreciation for this effort.

One member asked if the DTAC and pediatric communities should reach out to transplant programs who had initially expressed concerns about these requirements to let them know that their concerns are being addressed. The Chair and Vice Chair both mentioned that the DTAC had already sent a follow-up

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<sup>1</sup> [https://optn.transplant.hrsa.gov/media/3qeb2r5t/2021\\_07\\_30\\_dtac-peds-wg\\_mtg-summary.pdf](https://optn.transplant.hrsa.gov/media/3qeb2r5t/2021_07_30_dtac-peds-wg_mtg-summary.pdf)

letter and would be releasing a public comment proposal in just a few months, so it was likely not necessary to follow up until the proposal was available for the programs to comment on.

## **2. Public Comment Update**

UNOS committee liaison presented on the public comment feedback received so far for DTAC's current public comment proposals.

### Require Lower Respiratory SARS-CoV-2 Testing for Lung Donors:

Feedback:

- Almost entirely supportive sentiment, with two sentiments in opposition from OPOs
- Agreement – most lung centers ask for this testing anyway, support for policy
  - Protective of recipients, important test for recipient safety, especially given pandemic
  - Lung recipients should get best donor lungs possible
  - COVID-19 has significant impact to outcome of transplant. Ensure success for chance for second life for the recipients.
  - Given impact of COVID on lungs specifically, testing should absolutely done
- Non-lung recipients – any transmissions?
  - No proven/probable. Updated summary of evidence.
- BALs are challenging for OPOs
- Impact on utilization – if low level positive in lower respiratory sample
- Consensus on how long a period from known COVID positive status to donation represents transition to 'non-viable' status?
- Favor testing all potential donors (one comment)

Discussion:

One member asked if the comment about BALs being difficult to obtain was in regards to DCD donors or all donors. UNOS staff clarified that the comment was submitted as part of the regional meeting survey and that it did not specify further.

One DTAC pulmonologist mentioned that this is being performed for all donors, and that it afford them a much greater peace of mind when accepting organs.

Another DTAC pulmonologist and OPO member expressed concerns about the lack of data on sensitivity and specificity of different samples, tests, and platforms, and mentioned that there is a known large variability for NP swabs and there likely is for lower respiratory testing as well. The Chair asked the member if they had any suggestions for improvement, and the member said that the FDA should require sensitivity and specificity be submitted by manufacturers for all tests. The DTAC Chair agreed that this is vital information, but that it may be outside of the scope of the committee. He recommended the DTAC bring this concern to their FDA representatives.

A CDC member said that so far, there haven't been any cases of false negative lower respiratory sample tests with transmissions to any recipient in over fifty investigations. The CDC has only seen false negative upper respiratory tests, which is what led to the creation of this policy.

Another DTAC member stated that there's never a test that can 100% exclude a pathogen even if negative. The member also mentioned that the FDA does require a large number of tests for a lab to validate them internally, and that BAL samples must be diluted by the lab to process regardless and so there is still likely a large amount of variability. The member stated that this is an increase in screening capabilities and patient safety, but is only one piece of screening the donor.

The DTAC Chair agreed that it's not possible to build a system without transmissions, but that this policy does seem to be working as intended by increasing recipient safety. He also stated that the committee needs to balance the burden to the system, utilization, and what is practical as well.

### PHS Data Collection

Feedback:

- Supportive sentiment, with no sentiments in opposition
- ANNA supports, so does TAC (finds straightforward)
- Benefit in adding context to increased risk, but keep as simple as possible
- Most DRAI forms entered with discrete y/n donor risk questions
- OPO members expressed support for data collection, noting can provide significant value. Support for integration from EMRS and OPO data into DonorNet (streamlining data integration)
- Other PHS: blood volume for pediatric, financial burden
- Better safety net helping organs be used for best recipient

Post-Public Comment Potential Changes:

- 'yes, no, unknown' options to 'yes, no' (+ not applicable for pediatric questions)
  - Suggested change: remove 'unknown' so just 'yes, no' options
- Why: Interface with OPO team and consistency with EMR
- Implication of asking families of donors repeatedly with DRAI unknown questions
- Note: still have 'unknown medical history' as answer option whether donor has risk factors

Discussion:

Multiple members expressed agreement with removing the "unknown" option. No members expressed concerns.

One member stated that they've heard multiple concerns about insurance coverage of post-transplant testing, but acknowledged this is outside the scope of the current proposed data collection.

### **3. Public Comment Presentations**

The Committee heard three public comment presentations and had the opportunity for discussion.

#### Establish Continuous Distribution of Lungs (Lung Transplantation Committee):

Committee members discussed that an increase in travel for organ transport could mean that programs are encountering donors exposed to endemic diseases they are not familiar with and are not endemic to their area. They also discussed that some programs might be unfamiliar with certain tests, such as Strongyloides, if it's not commonly performed in their region. One member recommended that the committee consider guidance on screening and prophylaxis, or a resource about differences in test types and endemic diseases.

#### Update on the Continuous Distribution of Kidneys and Pancreata (Kidney and Pancreas Transplantation Committees):

Members agreed that the concerns from an infectious disease standpoint would be the same as with *Establish Continuous Distribution of Lungs*.

#### Data Collection to Evaluate Organ Logistics and Allocation (Operations and Safety Committee):

Members discussed the removal of the decline code for positive HTLV testing, and were in agreement that HTLV testing is almost never performed pre-procurement and so it is not a necessary organ decline

reason. The Operations and Safety Committee (OSC) Chair pointed out that this testing is still being performed for tissue donors, and that OPOs are required to report this to organ transplant programs if it returns positive, but this is long after organ procurement.

A DTAC transplant coordinator member asked where the data points related to organ check out would live. The OSC Chair stated that the committee had discussed this and for OPOs it would likely make sense to be in TransNet, but that for transplant programs it would be more difficult and may end up being at the time of waitlist removal on the transplant recipient registration (TRR). The transplant coordinator member suggested that this data would be helpful in real time for transplant hospital coordinators to see, to better track organ location. The OSC chair mentioned that this data point is meant to be used for analysis of organ logistics, not real time tracking, but that standardizing GPS tracking of organs would be ideal for real time updates.

Another DTAC member mentioned that some of the infectious disease refusal and decline codes are broad and unhelpful, such as "infection", and that it might be helpful to re-evaluate the nonspecific codes at a future date.

The DTAC Chair recommended that in addition, OPOs collect the location a donor is born and traveled, as it impacts the screening for endemic disease. The OSC Chair mentioned that this is collected as part of the Donor Risk Assessment Interview (DRAI), but is not captured discretely in DonorNet or the Deceased Donor Registration (DDR). A CDC member agreed that this would be useful information to track, as did multiple other committee members. The OSC Chair mentioned that currently the DDR does track citizenship status, and if the donor is a non-citizen it tracks country of birth, but this is limited. The DTAC Chair brought up that 90% of DTAC cases of Chagas or TB the donor has been a US citizen, and that a citizen and registered donor can still have risk factors.

#### **4. Require Lower Respiratory Testing for SARS-CoV-2 Monitoring Report**

UNOS Research Staff presented the 3 month post-implementation monitoring report on the committee's policies to require lower respiratory testing for SARS-CoV-2 in lung donors.

##### Data summary:

Summary of data review, if applicable

Attach data (slides or report) as exhibit/appendix/reference exhibit posted in SharePoint (if you intend for your slides/figures to be posted on the OPTN site, remember they must be **508 compliant**)

##### Summary of discussion:

Members discussed the trend of decreased overall utilization, and whether that was due to operational issues related to COVID-19 and workforce availability or the impact of the policy. Multiple members expressed that it's difficult to separate the two factors out and figure out what is the true driver. UNOS staff mentioned that there have been at least two lung transplant programs that have inactivated a large portion of their Waitlist and provided information to the COVID-19 survey, and that the high COVID-19 rates could be a complicating factor. A committee member commented that there have been regional problems with bed availability, especially in Florida and Texas, and that they knew of at least 7 lung programs that have had periods of inability to transplant patients. That member suggested the report look at regional variation in transplant volume.

The chair reported he was very high compliance with the policy, and that the 16 donors with negative upper respiratory testing and positive lower respiratory testing may represent potential prevented transmissions. He posed that DTAC should try to get as much data as possible on the 22 donors with positive lower respiratory testing, to inform the community of the capability of using organs and

minimizing any potential negative impacts this policy may have on utilization. Another member agreed, since it does seem safe to use these organs based on the preliminary data. They recommended that the committee create a resource on deceased donation for non-lung organs, but that there isn't quite enough information based on this report alone.

One member said that the kidney utilization seemed highest, even when the recipients have the lowest waitlist mortality. UNOS Research staff mentioned that heart utilization rates are typically 28-29%, and that the rate for donors with positive lower respiratory tests is slightly higher than normal.

Another member asked about outcomes of recipients with the positive lower respiratory tract testing, and at what point DTAC would no longer require the testing. The chair replied that there is a limitation to what DTAC can access in regards to false positive testing, since that isn't being reported to the OPTN. He recommended that DTAC obtain as much information as possible, through what data is already submitted on the DDR and in follow-up forms, to better assess the utilization of these COVID+ organs.

One DTAC member agreed, and recommended looking at waiting time for kidney recipients, to better determine how these organs are being utilized, as well as MELD score at time of transplant for liver recipients. He theorized that some patients who might not have access to other organs might be accepting these organs rather than continuing on the waitlist.

Another DTAC member suggested recipient COVID vaccination status and any prophylactic therapies they may have received, but the DTAC chair pointed out that this information is not currently collected.

Another member suggested that DTAC look at the time between the first positive COVID test reported and the time of transplant, to determine if these donors were being managed for a prolonged period of time prior to procurement.

A DTAC member suggested that the data report look at the individual OPOs procuring the organs and the regions in which they're allocating to.

Another member suggested looking at sequence numbers in allocation, and another suggested looking at left ventricular ejection fraction and history of coronary artery disease.

One member suggested looking at chest x rays and whether they had infiltrates. The DTAC chair said that may be difficult since it's not a discrete variable, and was unsure the committee would be able to access it.

One member asked whether or not DTAC could access the assays used for testing or cycle threshold values, and UNOS Research staff replied that this information isn't collected.

One member asked if all of these donor were referred to DTAC for medical peer review. The Chair and Vice Chair clarified that programs are only required to report suspected donor-derived transmissions, and so these would not be reported if there was no COVID-19 transmission.

## **5. Geographically Impacted Diseases**

### Tuberculosis (TB)

The CDC presented on a proven donor-derived tuberculosis case caused by tissue donation, as well as aggregate data for 47 organ donation related tuberculosis cases they have investigated. TB is the third most common potential donor-derived disease investigated, behind HBV and HCV, with the exception of COVID-19 cases during the pandemic.

CDC conclusions:

- M. tuberculosis was transmitted through bone allograft tissue from a single donor to at least 88 recipients in 15 states, resulting in significant morbidity and mortality
  - Donor likely had unrecognized disseminated TB with bone marrow involvement
- Current donor screening and tissue testing do not reliably detect M. tuberculosis infection or TB disease
- Further discussion is needed to improve TB screening for organ and tissue donors

CDC recommended next steps:

- Additional policies to further mitigate the risk of TB transmission through transplantation (organs or tissues) are necessary
- CDC is interested in considering role of additional PHS guideline vs another avenue for implementing laboratory-based donor testing
- Important considerations remain
- Mitigation of risk of latent TB among donors
- Testing methods, specimens and testing platforms
- Subgroup formation to assess possibilities

#### Summary of discussion:

One member brought up a concern that if an OPO performs TB testing, a donor hospital might require the donor to be kept in negative pressure or have respiratory precautions.

One member brought up that several donor management strategies have been previously shown to make certain screening methods for TB invalid and asked if there was any update to testing strategies. A CDC representative explained that there have been multiple issues across the cases they have investigated, including incorrect or incomplete information given to OPOs, a lack of donor history on TB, and latent TB testing information.

One member brought up that many tests for TB, including cultures, will take far longer than the time from admission to procurement to result. The member mentioned that pending tests at time of recovery can lead to discomfort in transplant hospital staff and underutilization of organs, even if the recipient can easily be treated with prophylaxis. Multiple members stated that latent TB testing wouldn't be a concern for donor exclusion, but for recipient prophylaxis and treatment. One member compared it to Strongyloides testing and the accessibility of prophylaxis.

One member stated that extrapulmonary or disseminated TB would likely be difficult to diagnose.

The Chair recommended the formation of a workgroup to investigate methods to mitigate donor-derived TB. Multiple members agreed.

#### Strongyloides and T. Cruzi

DTAC chair presented on endemic incidences, recommended screening practices, and donor-derived transmission of Strongyloides and T. cruzi.

#### Summary of Discussion

One member suggested that donors in Georgia and much of the Southeast US are already universally screened for Strongyloides. That member asked if this was only common in Appalachia, or if it was more universal across the country.

One member stated that a previous survey showed that practices are variable across the country, even if the donor has clear risk factors or resides in an endemic region. That member also stated that there was inconsistency in testing for Region 4, even with endemic risk.

Another member reported that even though risk is low in region 1, they screen most donors for Strongyloides, but have a fair amount of inconsistency on donors that are procured in other regions. The member reported that it doesn't affect their offer acceptance practices at all, so it wouldn't be required to be resulted at time of transplant, but that it does affect post-transplant care.

Multiple members agreed, and stated that education to the community would be important. One member posed that Strongyloides and T. cruzi should be included in the endemic diseases workgroup, and multiple other members agreed.

## **6. Closed Session Medical Peer Review**

DTAC members were divided into smaller peer review groups to review potential donor-derived transmission events. Group leads presented the adjudications and aggregated findings of the group based on the pathogen category after conclusion of discussion case agenda.

### Bacterial pathogens

High impact of gram-negative transmissions in kidney recipients and potential for anastomotic rupture. Members remarked on inconsistency in perfusate cultures and lack of clarity on the meaning of positive kidney perfusate cultures. Members discussed whether or not DTAC needed to review positive perfusate cultures, due to their high numbers of case reports with low reports of transmissions to recipients.

Members also remarked on the inconsistency in reporting for donor antibiotic use. One member reported that a previous DTAC study of gram-negative transmissions found that less than half of proven/probable transmissions had any reporting of antibiotic administration from any point in donor care. An OPO member said that this information should always be reported, but a transplant coordinator said that this is just in the medications/fluids tab and different OPOs have different consistencies in reporting it at all. One member reported that it makes it difficult to manage recipient care due to unknown susceptibilities, and that it can be hard to distinguish concerning positive urine cultures due to the volume.

### Fungal Pathogens

Members discussed the need for better fungal diagnostics due to the difficulties in detection for certain organisms.

### Viral Hepatitis

Members discussed the benefit of a resource on the comparative sensitivity and specificity of different testing platforms, and that while Ultrio is widely used for HBV/HCV testing it doesn't have the same level of detection as other platforms, especially for HCV.

Members also discussed the potential for a resource on retrospective testing of stored donor samples in cases with multiple recipients. One member said that OPOs may be reluctant to send the samples to transplant programs, and mentioned that there might be different levels of benefit depending on the number of recipients that might be affected by retrospective repeat testing, since the samples are finite and may be needed for other future uses.

### Other Viral Pathogens

Members discussed the potential need for repeat CMV tests if a donor initially tests negative, especially if the donor was hemodiluted. Members discussed center-specific practices for CMV testing post-transplant if a recipient was negative pre-transplant, with variable practices among committee

members. One member brought up that a fair number of pediatric candidates seroconvert over time, and that CMV testing needs to be repeated frequently in certain candidate/recipient populations.

#### Pathology

One pathologist member suggested that any Renal Cell Carcinoma (RCC) less than 2 cm at time of procurement and removed completely likely doesn't need to be reported to DTAC anymore. Another commented a concern in the length of time it took to get autopsy results reported.

#### Consent- Infection/Pathology

Consent packets were identified by potential transmissions reported due to donor findings with no signs or symptoms in any recipient at 45 days' post-reporting.

Members discussed trying to identify what Strongyloides reports required prophylaxis, and which recipients would not be at risk for transmission. Members also discussed the low risk of transmission of calcified histoplasmosis granulomas, with many members concurring that they only gave prophylaxis to lung recipients in those cases.

#### **Upcoming Meetings**

- October 5, 2021, 12 PM EDT, Teleconference
- November 2, 2021, 3 PM EDT, Teleconference



## Attendance

- **Committee Members**
  - Ann Woolley
  - Avi Agarwal
  - Charles Marboe
  - Debbie Levine
  - Dong Lee
  - Gary Marklin
  - Gerald Berry
  - Jason Goldman
  - Kelly Dunn
  - Michelle Kittleson
  - Lara Danziger-Isakov
  - Raymund Razonable
  - Ricardo La Hoz
  - Sarah Taimur
  - Stephanie Pouch
- **HRSA Representatives**
  - Jim Bowman
- **CDC Staff**
  - Ian Kracalik
  - Noah Schwartz
  - Pallavi Annambhotla
  - Rebecca Free
  - Sridhar Basavaraju
  - Sue Montgomery
- **FDA Staff**
  - Brychan Clark
  - Scott Brubaker
- **UNOS Staff**
  - Abby Fox
  - Anne McPherson
  - Cassandra Meekins
  - Courtney Jett
  - Darby Harris
  - Elizabeth Miller
  - Joann White
  - Leah Slife
  - Lindsay Larkin
  - Sandy Bartal
  - Sarah Booker
  - Susan Tlusty
- **Other Attendees**
  - Chris Curran
  - Erika Lease
  - Jim Kim