

OPTN/UNOS Ad Hoc Disease Transmission Advisory Committee
Meeting Minutes
October 16, 2018
In-Person Meeting, Chicago, IL

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Introduction

The Ad Hoc Disease Transmission Advisory Committee met in-person in Chicago, Illinois on 10/23/2018 to discuss the following agenda items:

1. Policy Oversight Committee (POC) Update
2. HOPE Act Variance: Project to Expand to Other Organs
3. Multi Drug Resistance (MDR) and Pathogens of Special Interest List Review
4. Guidance on Effective Practices for Broader Sharing
5. Centers for Disease Control and Prevention (CDC) Case Review
6. US Public Health Service (PHS) Increased Risk Guideline: CDC analysis and future considerations
7. Manuscript, Abstract and Case Study Reviews
8. Confidential Case Review
9. New Business and Closing

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

1. Policy Oversight Committee (POC) Update

Summary of discussion:

The Committee received an update on the Policy Oversight Committee (POC) from the DTAC vice chair who serves on this group. All vice chairs serve on the POC. Their job is to review all projects submitted by Committees. They also review all proposals before they go out for public comment.

Recent POC work has included:

- Helping develop a response to the Health Resources and Services Administration (HRSA) regarding the use of Donation Service Areas (DSAs) and Regions
- Recommending six proposals for public comment (August-October 2018)
- Recommending one proposal for special public comment (October-November 2018)
- Reviewing and recommending two new committee projects

The POC recommended that the Living Donor Committee project on Clarifications on Reporting Maintenance Dialysis and the Operations and Safety Committee guidance project on Effective Practices for Broader Organ Sharing move forward to the Executive Committee.

2. HOPE Act Variance: Project to Expand to Other Organs

The Committee discussed the current results of the HIV Organ Policy Equity Act (HOPE) Act for kidney and liver transplants and the possibility of expanding the project to other organs. The HOPE Act was enacted on 11/21/13 to allow transplants to take place from HIV positive donors to HIV positive recipients under research protocols. On 11/23/15, the Secretary of HHS published criteria for conducting research and revised the Final Rule accordingly. In addition,

the OPTN revised organ allocation policy and system programming to allow participation in the OPTN HOPE research variance for kidney and liver organ transplantation.

Data summary:

The following HOPE Act statistics were recorded as of October 5, 2018:

There were 48 approved OPTN transplant programs across 27 transplant hospitals.

Kidney: 29 programs (27 deceased donor; 2 living donor)

Liver: 19 programs (16 deceased donor; 3 living donor)

221 candidates (202 kidney and 19 liver) were waitlisted for an HIV positive kidney or liver transplant at a total of 22 programs

Through January 1, 2016-October 5, 2018

- 44 HIV positive deceased donors recovered throughout the US
- 39 had at least one kidney recovered
- 28 had a liver recovered
- 39 transplanted donors
- Some could be false positive donors

As of October 14, 2018, there were:

87 transplanted organs at 15 programs

- 60 kidneys (1 en-bloc kidney)
- 27 livers (4 were simultaneous liver-kidney transplants)

Summary of discussion:

One topic of conversation among the Committee was the issue of inconsistent state laws regarding HIV positive transplants. Some state laws still ban transplantation of any HIV positive organs in accordance with the previous prohibition once in the National Organ Transplant Act (NOTA). An OPTN/UNOS staff member explained the next steps and schedule of the policy process that would allow for transplantation of all HIV positive organs according to the HOPE Act criteria. A discussion arose among the Committee regarding the merits of expanding the HOPE Act to increase the number of transplants. Expanding the HOPE Act would prevent possible organ wastage that occurs for HIV positive organs that are currently ineligible for transplantation and incapable of matching in UNetSM. A committee member brought up the issue of organs that test HIV positive but turn out to be false positives and are not able to be allocated in a regular match run. After some discussion regarding the possibility of validating that some HIV results are false positives, the Committee agreed that the issue was out of scope for the current project editing HOPE Act policy and would be better dealt with by a different project at a later date.

Next steps:

The project will proceed to the Policy Oversight Committee on 10/23/2018 and then to the Executive Committee on 10/26/2018. If both committees approve the project, the DTAC will develop official language for a public comment proposal, which will be due on 12/14/2018. The spring public comment period would be open from 1/22-3/22/2019. The Committee would then review public comment and finalize the proposal by 4/19/2019. The OPTN/UNOS Board of Directors (BOD) would vote on final policy language at their summer meeting on 6/10/2019 to allow the HOPE Act variance to be extended to other organs for transplant programs applying

for the variance that meet established criteria. UNetSM programming would need to be done for policy implementation to follow.

3. Multi Drug Resistance (MDR) and Pathogens of Special Interest List Review

Summary of discussion:

The Centers for Disease Control (CDC) presented data and general information to the committee regarding Carbapenemase-producing organisms (CP or CPOs) and other Multi-Drug Resistant organisms (MDRs or MDROs). The primary question the committee discussed was whether CPOs should be included in the Pathogens of Special Interest list maintained by the DTAC. The second half of the discussion was focused on reviewing and making edits to the Pathogens of Special Interest list.

Data summary:

Data was presented to the committee by the Centers for Disease Control (CDC). The first graphical depiction that the CDC presented was regarding the international spread of Carbapenemases and how in turn, their spread can increase the percent carbapenem-resistant. Each country had a statistically significant increase across the five countries shown, including Greece, Israel, Cyprus, Italy and Romania.

Within the U.S., data was shown that illustrated how *Klebsiella pneumonia carbapenemase*-carbapenem-resistant *Enterobacteriaceae* (KPC-CRE) found in the U.S. has spread from two states in 2001 to all U.S. states, Washington D.C and Puerto Rico by 2017. However, the spread of KPC-CRE is nonlinear and diverse within all regions, whereby regions or cities differ significantly in the number of KPC-CRE cases that are identified.

Another area of data presented was the CRE and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) data that was tested from January 1, 2017 to December 31, 2017. From the data, KPC was the most common CRE case. For CRPAs, the *Verona integron-encoded metallo-β-lactamase* (VIM) represented the highest number of cases. Further data presented highlighted that overall, the number of patients with CP-CRE reported since January 1, 2018 has spread to numerous states throughout the U.S. Other data presented the epidemiology spread of patients with CP-CRPA within the U.S. as of January 1, 2018.

Summary of discussion:

What are Carbapenemase-producing organism (CPOs)?

CPOs are gram negative bacteria that are resistant to certain types of drugs due to their structure and epidemiology. Carbapenemase genes are often on mobile genetic elements that can be transferred among other gram-negative organisms and increase potential for epidemic spread.

What do we already know about the epidemiology in the United States?

There are five Carbapenemase-producing organisms that are of public health concern in the U.S. These five organisms are as follows: KPC, New Delhi *metallo-β-lactamase* (NDM), VIM, 'Active on imipenem' (IMP), and 'Oxacillin-hydrolyzing' (OXA). These five organisms are the top organisms that the CDC is currently tracking nationally.

What is the CDC doing to control the spread?

Currently, the CDC is using a systematic approach to slow the spread of novel or rare multi-drug resistant organisms or mechanism through aggressive response to one or more cases of targeted organisms. Such organisms include "nightmare bacteria" (such as CRE and CRPA)

and *Candida auris*. The CDC is also coordinating public health initiative, emphasizing early detection and quick action, and using detailed guidance for responses.

The CDC has a laboratory network that tests specifically for multi-drug resistant organisms. This network is present in all fifty states and Puerto Rico. Any positive results for CPOs are sent to the health department, where the facility must then follow CDC recommendations for infection control, identify other patients at risk and consider on-site assessment to review infection control policies. However, there are some isolates that are referred for further testing to determine new mechanisms of resistance and any additional antimicrobial susceptibility testing.

Transplants and CPO transmission

It is currently unknown how CPOs are commonly transmitted as a result of transplants. Among transplant donors, CPOs are dependent on past medical history, exposure to healthcare, location and travel risk factors. As of right now, there are currently no recommendations for screening transplant donors, even in areas where CPOs might be endemic. Another question the CDC has is whether transmission through a solid organ transplant poses an infection control risk for a transplant recipient hospital.

There have been a few studies that have been conducted to answer the questions regarding CPO transmission and organ transplantation. The most recent study focused on screening for CPOs and MDRs in fecal samples from the time of transplant candidate enrollment to one year post-transplant. This study found that out of the 998 stool samples collected, MDRO colonization was detected in 86 patients at least once and was significantly associated with subsequent MDRO infection. Out of this study, it was also found that KPC was detected in 63 of the 96 isolates and CRE colonization was detected approximately 24 days post-transplant. Furthermore, 3 of the 9 patients colonized with CRE developed an infection. Other studies highlighted the spread of CRE and MDRO transmission through organ transplantation.

Recently, the CDC was notified by a state department of health regarding a potential carbapenem-resistant *Acinetobacter baumannii* (CRAB) case where post-procurement cultures were positive in one organ but not the others recovered and transplanted. The CDC has had experience with a prior case where a transplant recipient developed a CRAB infection post-procurement along with a surgical site infection and subsequently died.

General Discussion

One committee member asked how OPOs could track and report CPOs or MDRs since their primary reporting mechanism is based on sensitivity.

Another committee member asked if OPOs always get susceptibility testing. The answer given was negative because some hospitals may throw out the cultures of a patient who has died or has been discharged. There have been many issues particularly with urine cultures.

One member asked if all the laboratories (labs) around the country are required to report these results and statistics. All states maintain reportable disease lists that must be reported to state health entities under state laws. The CDC also maintains a national notifiable list that includes CPOs. CDC receives reports from 57 jurisdictions but reporting to CDC is voluntary not required by federal law. CDC does sometimes become aware of potential infectious disease cases that involve transplant patients through the state to CDC reporting mechanism. CDC checks with UNOS DTAC staff to ensure that these are also being reported through the policy-required OPTN system.

There was general agreement among members that MDRs have been increasing across the U.S. and that they needed to be addressed. One member pointed out that this increase could be due to a mismanagement in antibiotics between the transplant hospital and OPOs. In this

member's opinion, when reviewing charts for antibiotic usage, they find it surprising that some patients are on antibiotics for long periods of time. The issue of prophylactic antibiotics has not really been addressed by OPOs. There is no regulation for monitoring antibiotic usage for many transplant hospitals, especially related to donation after circulatory death (DCD) donors. Some committee members pointed out that antibiotics such as vancomycin can be nephrotoxic, which should be monitored. Another point was that some OPOs conducted their own cultures, which means that there are multiple results that could impact the prescription of antibiotics.

From an OPO standpoint, many prophylactic antibiotics are negotiated between the different organs. Another question asked was whether or not if a patient is known to have resistance to any of the prophylactic antibiotics given to DCD donors. Many members pointed out that it is very difficult to get information on infections from transplant hospitals and OPOs. One committee member proposed the idea of putting together a subcommittee that could delve further into the MDRs and their effect in transplantation. There was general agreement that this was needed and that they could potentially meet in January 2019.

Overall, there were many questions surrounding the processing and notifications of MDR lab results between OPOs and transplant hospitals regarding donors and recipients.

Pathogens of Special Interest

The committee discussed adding Enterovirus N71 and acute flaccid myelitis (AFM) also referenced as polio-like illness or paralysis to the Pathogens of Special Interest list. There was general agreement among committee members that these changes were acceptable. This list is specifically for conditions identified in a deceased donor, because there had been over-reporting of positive donor cultures to the OPTN that did not need that level of follow up. OPTN policy requires that all positive cultures be reported to transplant programs but there is a subset that are also required to be reported to the OPTN. This subset includes items on the Pathogens of Special Interest list. If the organism is identified in the donor, then it could be transmitted to organ recipients. Members discussed that there may be a need to produce another special communication as members felt that some in the community might not be aware of this list. It was noted that this list is not all-inclusive and the committee can revise it as needed. OPTN policy requires that DTAC review the list at least every two years.

It was suggested that a small working group be formed in order to analyze the logistics of how transplant centers and OPOs report the pathogens on this list. The CDC would work with the committee group in order to go through the logistics, such as how the pathogens are identified and results reported.

CDC clarified that their concerns discussed today were not necessarily related to "antibiotic stewardship" but that the CDC is also analyzing how the organisms are spread from one patient to another.

Next steps:

The committee agreed to form two smaller committee groups (or one group) to analyze the use of antibiotics within the transplant system and to analyze the logistics of pathogen reporting to the OPTN and CDC.

4. Guidance on Effective Practices for Broader Sharing

Background:

The project to offer guidance on effective practices for broader sharing was started by the Operations and Safety Committee (OSC). DTAC volunteered to develop a section that deals

with potential impacts and recommendations related to infectious diseases and policies being developed to share organs more broadly.

Summary of discussion:

As new policies for broader sharing are developed, there will be new partnerships between transplant hospitals and OPOs. DTAC was asked to give feedback on the project to offer guidance on effective practices for broader sharing.

The guidance is projected to go out during spring 2019 public comment. The target audiences are the Ad-Hoc Geography and organ-specific committees as well as OPOs and transplant hospitals adopting revised allocation policies.

The project will offer guidance on a vast array of topics. It is important for DTAC to consider how broader sharing and new partnerships will effect transmission of infectious and non-infectious disease. DTAC must also recognize that some OPOs are screening donors for seasonal and geographic endemic diseases, and these organs are now being transported to different areas. Transplant hospitals need to be aware of these screening practices, what the results mean for the recipient, and the ways to mitigate the infection to prevent transmission. Transplant programs also need to recognize that the OPOs that they are now working with may not have the same screening process as the OPOs they typically work with. The absence of a positive test does not mean the donor is negative, it may just mean the organ was not screened. Conversely, a transplant program may turn down an organ that has tested positive for an infectious disease, even though it is possible to use the organ.

One committee member spoke about a survey put out by the Association of Organ Procurement Organizations (AOPO) that asked OPOs about screening for Strongyloides. Thirty-three OPOs responded. Five OPOs screen all donors, eight OPOs conduct selective screening, and 20 OPOs do not test but were going to discuss it in the future.

One committee member mentioned that there needs to be more education about infectious disease across the transplant community because some transplant centers have pushed back on the validity and usefulness of screening results. DTAC and the transplant societies can do more education of transplant centers. Another committee member was surprised that there is no requirement that all OPOs have an infectious disease advisor. The Chair suggested talking to AOPO. It was noted that this would be a helpful role but that there are legal ramifications for making binding recommendations for an official advisor to an OPO and therefore complicates the issue.

One committee member noted that how transplant centers receive screening information is also important and should be part of DTAC's educational commitment. UNOS staff has requested that the UNOS communications department put together a regular information outlet to help educate the community on infectious disease topics. However, UNOS staff needs insight from the Committee on how to effectively reach those that need the education. Regional meetings are a good opportunity for education because they occur regularly and education needs to be a continuous process. Some regions already have time during their meetings for a DTAC update and all regions have the opportunity to receive an update. However, Committee members would need to be willing to go to regional meetings to present. This would be an extra commitment and is not reimbursed by UNOS.

One committee member suggested the DTAC update should be in a case review format at the regional meetings. The Chair approved of this idea and asked committee members to see if they will be able to attend their next regional meeting. Data would have to be presented in aggregate not as individual cases to maintain confidential medical peer review protections.

One committee member commented that there should be a way for transplant centers to go online and see each OPO's screening policies. There are only 58 OPOs and only a certain number of diseases that are screened for, so this would not be a complicated process.

UNOS staff noted that the infectious disease screening page is also being re-visited with a previously approved proposal to change the OPTN extra vessels label. There has been discussion to add as other conditions. DTAC was previously consulted. Strongyloides is planned for addition to the infectious diseases screening page. Fields for tests not required by OPTN policy will not be mandatory to complete. DonorNet® will have more capacity to show screening results in Q2 of 2019.

One committee member mentioned that the donor highlights section is not a good place to put screening information because there is a lot of information there and the results might get lost. It might be worthwhile to have an infectious disease highlights section instead.

The Chair voiced support for having UNOS communications department help the Committee promote shorter, more frequent updates.

Next steps:

UNOS staff will work with Communication department to create a standing regular educational feature or outlet where DTAC can post relevant and timely materials on infectious disease and malignancy findings, screening practices, and other effective practices.

Committee members will consider if they are available to present at Regional Meetings.

5. Centers for Disease Control and Prevention (CDC) Case Review

Summary of discussion:

The Committee conducted a closed-session for findings and case adjudication of CDC investigated potential donor derived transmission events (PDDTEs) under confidential medical peer review.

6. US Public Health Service (PHS) Increased Risk Guideline: CDC analysis and future considerations

Summary of discussion:

The purpose of the discussion is to talk about concerns and potential next steps with the current definition of US Public Health Service (PHS) Increased Risk donors.

Data summary

Under current OPTN Policy following the PHS guideline, 26.3% of deceased donors in 2017 were designated as increased risk which then requires a specific informed consent process after the organ offer and before transplant.

Summary of Discussion

One committee member said that the current system for identifying increased risk donors is out of date and was developed prior to the use of the Nucleic Acid Amplification Testing (NAT). The committee member stated that it is time to re-examine the guideline.

The Centers for Disease Control and Prevention (CDC) DTAC ex-officio member presented data on the prevalence of increased risk organs. At the previous in-person DTAC meeting (March 29, 2018), the committee discussed the 2013 PHS guideline and whether there was room for improvement. In June 2018, the American Society of Transplant Surgeons (ASTS) sent

a letter to the CDC about revising the guidelines as well. Two specific issues with the guidelines were raised:

1. Are the guidelines causing adverse outcomes, such as more discards, underutilization, or reduction in match efficiency?
2. Is it factually correct to designate a donor increased risk for behavior that occurred up to 12 months prior to donation?

There has been a number of papers published that examined the increased risk designation and its impact on utilization and discards. Several studies have reported that there is underutilization of increased risk organs. However, some of these studies grouped increased risk organs together with donors who are HCV sero-positive so it is noted that it is unclear if the organ was not used because it was designated as increased risk or because it was HCV sero-positive.

The CDC and HRSA used OPTN donor demographic data to look at the proportion of increased risk donors. The number of increased risk donors has grown over the past five years largely due to intravenous (IV) drug use. Approximately 15% of increased risk donors had a positive NAT test for hepatitis C (HCV), while only 1.1% of standard donors tested positive for HCV. This shows that there is inherent value in identifying donors who potentially have risk factors for HBV, HCV, and HIV. CDC data were analyzed. Additional data collected by CDC as part of DTAC investigations suggests that the majority of recipients who experienced a donor-derived disease HBV or HCV transmission survived with a functioning graft in the setting of anti-viral therapy. These recipients survived because they were quickly treated after transplant due to the PHS guideline identifying at-risk recipients and the OPTN policy requirement for post-transplant recipient testing following receipt of an increased risk organ. Altogether, data show that increased risk donors are more likely to transmit HCV through transplant, but it is not associated with graft failure or death.

One committee member noted that 8% of donors had intoxication as mechanism of death and a history of IV drug use. The CDC did not have the data showing why donors were designated as increased risk. The OPTN does not collect the reasons for increased risk status. The CDC is also starting to analyze if increased risk organs are underutilized. While it does look like there is some underutilization, the reasons for organ discard appear as heterogeneous as standard risk organs. There is large variation in the use of increased risk organs by transplant program, even within the same region.

One committee member asked the CDC ex-officio member about the impact of increased risk donations on the pediatric population. The number of increased risk donors used in pediatrics is low, so the CDC focused on adults for this analysis.

The next question identified above is whether the guideline could be refined to be more accurate. The CDC is building mathematical models using several different inputs to predict the probability of undetected infection in donors. The risk of undetected donor HCV or HIV after 30 days following behavior is close to zero. The risk will likely never go to exactly zero.

It was expressed that the increased risk designation is probably not doing harm, but may be causing disparity in organ acceptance rates across programs. It was also stated that the guideline is beneficial because it is effective at identifying a population that has a higher rate of infectious disease. However, the guideline recommendations can be improved. CDC staff expressed that there would likely be support for shortening the current 12 month time frame used to designate donors as "increased risk." CDC staff noted that individuals have expressed concern over the term "increased risk," and they are willing to consider alternate terminology that evokes less of an emotional response.

One committee member brought up OPO donor worksheets. These worksheets do not actually say “increased risk”, but do have “Donor Medical History” and “Donor Social History” as reasons for organ discard or turn-down. Another committee member stated that the reasons for turn-down are not helpful because they are almost always “Donor Quality,” which could mean many things.

A committee member stated that there is harm being done by the increased risk designation because programs will accept an increased risk organ but the recipient will turn it down, and the program will be forced to reallocate the organ. Members commented that there are too many donors identified as increased risk. A shorter evaluation interval would have fewer donors designated as increased risk, which would increase utilization.

An American Society of Transplantation (AST) representative stated that the issue lies in the use of the term, “increased risk.” It is important to come up with a term that conveys the appropriate amount of information to potential recipients at a time when they are willing to hear such information.

A committee member noted that often the code entered for turning down an organ does not reflect the reason discussed by the transplant team. The same committee member asked if CDC staff had looked at where increased risk organs were being allocated on the match run as opposed to standard risk organs. The committee member suspected that the increased risk organs are being allocated to recipients lower on the match run. The CDC did look at this and found that an increased risk organ was typically allocated only one place lower on the match run.

A committee member noted that a number of recent papers have shown that the increased risk designation is associated with a higher chance of organ discard. However, the post-transplant outcomes are equivalent with standard risk organs.

Another committee member stated that many recipients are misinformed and do not understand what increased risk truly means. The committee member noted that this misperception may be more pronounced in disadvantaged and low socioeconomic status populations.

It is also possible that a large number of donors are designated as increased risk because the individual providing the information for the deceased donor may not know about their social or medical history. A shorter evaluation interval may allow for the collection of more accurate information.

A committee member asked CDC staff if they had examined any variance in the behavior of recipients who received an increased risk organ. The PHS guideline included precise recommendations on how recipients of increased risk organs should be followed. OPTN policy only requires that transplant centers have a follow-up protocol for HIV, HBV, and HCV testing but policy does not prescribe what that protocol needs to be. There may be an opportunity to improve follow-up protocol for recipients of increased risk organs.

The Chair asked CDC staff if they would like assistance in reviewing the guideline. CDC staff stated that the US Department of Health and Human Services (HHS) has an Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) that provides advice on blood, organ, and tissue safety policy. This advisory committee will convene in 2019. At that time, the PHS agencies will present data and solicit input. But in advance of that, the CDC would like to speak with various transplant stakeholders in regards to alternative terminology, feedback on data, and what the guideline recommendation revisions should look like. The ACBTSA would put out a proposal for modifying recommendations using the federal public comment process. The CDC would like the process to be as collaborative as possible. It is

unlikely that this will entail a full scale revision of the guideline but rather an update on some of the recommendations.

Committee members noted that the blood and tissue communities likely view risk differently than the organ transplant community so it is important to get robust input from transplant community. Blood and tissue do not have as an acute and vast shortage as solid organ does.

The Vice Chair asked if the CDC would be able to predict the percent of organ donors who would be designated as increased risk after any the changes have taken effect. The CDC staff were unsure. However, the Chair showed a graph that depicted the increased prevalence of IV drug users over the previous seven years. A committee member also stated that their OPO is seeing more increased risk donors due to jail time and dialysis.

Next steps:

CDC will solicit input from DTAC and the broader transplant community on potential revisions to the PHS guideline recommendations prior to the ACBTSA meeting in 2019.

7. Manuscript, Abstract and Case Study Reviews

The Chair reviewed data and presented an update on the presentation/abstract/manuscript status for the following aggregate data case review studies:

- A. Peanut allergy
- B. Renal Cell Carcinoma (RCC)
- C. 10 year DTAC analysis
- D. Cryptococcus
- E. Strongyloides
- F. Hepatitis C (HCV)
- G. Human Herpes Virus (HHV)8
- H. Vascularized Composite Allograft (VCA) and infectious disease
- I. Granuloma

Data Summary and Summary of Discussion:

- A. *Peanut (Nut) Allergy: "Donor-derived Nut Allergy after Solid Organ Transplantation-Analysis of the OPTN/UNOS DTAC"*

This abstract was presented at the International Society for Heart and Lung Transplantation (ISHLT) and at the American Transplant Congress (ATC). The manuscript is under development in conjunction with a pediatric allergist. The major findings showed that transmission of nut allergy occurred from 6 donors into 27 recipients. All donors had a known peanut allergy and 4 of those same donors died from anaphylaxis. One recipient died from anaphylaxis following nut ingestion. Lung and liver recipients had the highest rates of transmission.

A member stated that because the donors had known peanut allergies these could have been avoided. In addition several members asked questions and gave examples illustrating how this is a very under-reported condition.

- B. *Renal Cell Carcinoma (RCC): "Outcomes from donors with reports of suspected and proven renal cell carcinomas (RCC)"*

This was presented at ATC 2018 and the paper submitted to the American Journal of Transplantation (AJT) in September 2018. The data were from OPTN reports from January 2008 to December 2016. The findings stated that 154 out of 174 donor

suspected cases reviewed did have RCC. In addition 65 of deceased donors had both kidneys discarded of which 4 were later found to be benign, however none of the 80 non-renal recipients developed the disease. 39 of these cases had both kidneys transplanted, and 29 of those had a suspicious lesion at procurement that was later biopsied/excised. Ten cases that had RCC were found by recipient report of the disease. Two of these cases were not preventable.

In 41 cases the kidney with RCC was discarded and the contralateral kidney was used. Out of the 41 cases, only 1 donor RCC was suspected but not confirmed. In the 9 cases of living donors, 5 of them had a lesion that was resected at procurement and no disease was shown in the recipient. The last 4 underwent cryoablation, partial or total nephrectomy. In conclusion, transplant teams should consider more use of contralateral (to RCC kidneys) kidneys or perhaps transplant team judgments are correct due to the low numbers of transmission.

DTAC concluded that there should be no unexpected transmission from donors with a confirmed RCC found prior to transplant. Secondly, finding a small RCC allows more time for reliable pathology and in many cases the tumor can be excised thus treated the disease by removing the malignancy without any consequence to the recipient. A.

One member stated they will alert the committee when this paper gets published. Several members commented on the benefits of using contralateral kidney and the affected kidney after RCC excision. A member also stated that this case fits into the OPTN/UNOS strategic goal of increasing transplants.

C. *10 year DTAC analysis: "A Decade of Donor Derived Disease: A report from the OPTN/ UNOS DTAC 2007-2017"*

This paper was led by prior and current leadership on behalf of DTAC. There was a poster presentation at ATC 2017 and the paper is currently in progress. Overall, 2181 cases are being included in the analysis and all have an adjudication.

D. *Cryptococcus: "10 years of DTAC experience with Donor- Derived Cryptococcus transmission in solid organ transplantation in the US"*

This abstract was presented at ID Week. There were 46 cases reviewed with 8 labeled possible and 10 with Intervention without Disease Transmission (IWDT). There were 8 donors labeled with proven/probable *Cryptococcus* affecting 22 recipients. Fourteen recipients were designated as proven/probable. One recipient dies and 10 had severe consequences (e.g. prolonged hospitalization). Three recipients did not have any severe outcomes from the donor-derived infection.

There were several conclusions from the study. First, donors infected with *Cryptococcus* can infect multiple solid organ transplants (SOTx) recipients and donor-derived *Cryptococcus* continues to have high morbidity in post-transplant settings. Any *Cryptococcus* infection within three months post-transplant, might be donor related and should be reported to the OPO and the OPTN per policy. Other conclusions were that not all yeasts in donor blood cells (BCs) are *Candida*. In addition, a consideration for donor testing for *Cryptococcus* should be made when stroke or other central nervous

system (CNS) events occur and these events would otherwise be clinically rare in the donor.

A member summarized a take home message for the committee and stated that the listed mechanism of death in the donor (with *Cryptococcus*) was not as severe as the actual description of how the donor dies. In addition another member stressed the importance of early recognition test/ questions for *Cryptococcus* so it can be treated early. Other members brought up more examples. Another member stated to not underestimate the conclusion that not all yeasts in donor blood cultures are *Candida*.

E. *Strongyloides: Strongyloides Review of cases*

DTAC is working on a review of all *Strongyloides* cases following a noted increase in reporting in the past two years. There are 86 cases under review and 78% of those 86 have had data abstraction performed and entered in REDCap. DTAC plans to submit an abstract for the 2019 ATC. The deadline has been changed from December 1st to November 30th.

F. *Hepatitis C (HCV) "Donor Derived Hepatitis C in an era of increasing intravenous drug use"*

This abstract was presented at the 2017 ATC is now published in *Clinical Transplantation*. The findings showed that 15 out of 95 reviewed cases were Proven/Probable. The study was conducted due to the increased number of donors with intravenous drug use (IVDU) in 2016.

G. *Human Herpes Virus (HHV)8: "Donor Derived Kaposi Sarcoma in Organ Transplant Patients: A report from OPTN/UNOS DTAC"*

A poster was presented at ATC 2017 and paper is almost completed. The suspected cases reviewed are from 16 donors whose organs were transplanted into 59 recipients. During adjudication, 5 donors were given Proven/Probable designation and 4 donors were labeled Possible. There were 5 deaths in total. HHV8 the virus associated with Kaposi Sarcoma is a rare event in the US organ transplant recipient population. Risk for HHV8 was identified in 8 out of 9 donors who were born in the Caribbean or Central America and/or with IVDU or men who have sex with men (MSM). In conclusion, HHV8 serology should be considered in donors with risks and clinicians should be on heightened alert post-transplant.

One member suggested that 2017 and 2018 case data be added to the study. Several members commented on how Kaposi sarcoma is not just a cancer but viral as well and hoped that the paper would help illustrate that fact.

H. *Vascularized Composite Allograft (VCA) and infectious disease*

The VCA oral presentation was not discussed.

I. *Granuloma:*

This project has taken longer than anticipated due to staffing and DTAC member changes. Out of 190 cases, 28 cases have had data abstracted and entered into a spreadsheet. It was suggested to hone in on a subset of cases to analyze in order to

make it more manageable and to put the data into REDCap. Another member mentioned that the granuloma category is too broad as it currently includes endemic fungal infections and micro bacteria. The group decided to focus this review on tuberculosis cases and the CDC has offered to assist given their previous presentation at the prior in-person meeting. The plan is to pull the summary together and submit an abstract for 2019 ATC.

Summary of Discussion:

The committee further discussed the need for more Infectious disease staff representation earlier in the process on the donor side. The committee wants to pursue this issue to understand where they can improve this process and ultimately prevent transmissions. There was some discussion about CMS requirements, potential medical liability, and other concerns. This issue will be further researched for future DTAC discussions.

Next steps:

- Finish development of abstracts, posters, oral presentations and manuscripts
- Submit for HRSA approval as required
- Present findings through print and oral opportunities

8. Confidential Case Review

Summary of discussion:

The Committee conducted a closed-session for findings and case adjudication of OPTN reported potential donor derived transmission events (PDDTEs) under confidential medical peer review.

9. New Business and Closing

Summary of discussion:

No new items were brought forward for discussion.

Upcoming Meeting

- November 26, 2018 (Monthly teleconference and case review)