Welcome to the DTAC News. This newsletter is brought to you by the OPTN/UNOS Ad Hoc Disease Transmission Advisory Committee and is meant to be a resource to the transplant community toward avoiding potential donor-derived disease transmission.

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FROM THE EDITOR…

We received a warm welcome from the transplant community for our first newsletter, and hope that you will find this second edition of the DTAC News to be equally as interesting and helpful as a resource. The DTAC has had a busy year, successfully completing its rewrite of OPTN Policies 2.0 and 4.0 and making plans to begin a number of educational efforts that will result in guidance documents for the community based upon what it has learned during its review of reported potential donor derived disease transmission events.

Wishing you and yours a bright holiday season and a happy new year!

Lewis Teperman, MD
Editor

POLICY 2.0 & 4.0 REWRITE APPROVED BY THE BOARD

The DTAC’s proposal to clarify or improve current OPO and transplant center requirements for screening for, communicating and reporting all potential or confirmed donor-related disease and malignancy transmission events went out for public comment in March 2010. Changes to Policies 2.0 and 4.0 were approved by the Board of Directors in November 2010, with implementation scheduled for January 10, 2011.

Key areas of change include:

- All blood samples obtained and used for potential donor screening tests required by policy must be assessed for hemodilution using an FDA-approved hemodilution calculation. If a qualified (non-hemodiluted) specimen is not available, transplant centers should be made aware of this.
If your OPO or transplant program would like more information regarding hemodilution, please review the FDA’s current guidance regarding hemodilution. See appendices 1-3 for an example of a hemodilution calculation and additional information regarding its use: [http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm073964.htm#DONORTESTING:GENERAL1271.80](http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm073964.htm#DONORTESTING:GENERAL1271.80)

- OPOs and transplant programs must develop a process for identifying a patient safety contact and follow this process for receiving potential disease transmission notifications and any related communication with the OPTN.
- OPOs must establish and implement a process to report all positive screening or diagnostic tests received to the transplant center’s patient safety contact within 24 hours of receipt by the OPO. The OPO must report updates such as identification of organism and sensitivity to the transplant program(s) as the OPO receives the information.
- Minimum requirements for informed consent of recipients regarding risk of transmissible disease.
- Changes to OPO and transplant program responsibilities related to reporting potential donor-derived disease transmission events.

Please take a few moments to review all of Policies 2.0 and 4.0, as many other sections of policy have been moved or rewritten: [http://optn.transplant.hrsa.gov/policiesAndBylaws/policies.asp](http://optn.transplant.hrsa.gov/policiesAndBylaws/policies.asp)

**COCCIDIOIDOMYCOSIS AFTER ORGAN TRANSPLANTATION**

Coccidioidomycosis is a fungal infection typically found in the southwestern United States, northern Mexico, and parts of central and South America. Coccidioidomycosis can result from: inhalation of the organism after soil exposure; reactivation of a latent infection; or on rare occasion, it can be donor-derived from an infected organ or from the blood within the organ. Coccidioidomycosis can be difficult to recognize because of its variable (sometimes asymptomatic) presentation and overlapping symptoms in prospective donors with their inherent confounding medical/surgical processes and nosocomial processes.

From January 2009 through December 2010, nine cases of potential donor-derived Coccidioidomycosis transmission were reported to the Patient Safety System. All were unexpected and four deaths were attributed to transmission. Early antifungal therapy in some of the recipients averted infectious complications. Positive *Coccidioides* transmission was confirmed after completion of serology testing on archived donor serum or by culture and pathologic confirmation from suspicious donor lung nodules.

Key points to consider:
- The recognition of active or chronic donor coccidioidomycosis may be misinterpreted for other clinical syndromes. For example, pulmonary *Coccidioides* infiltrates may be incorrectly attributed to other causes of lung infiltrates including pulmonary edema, atelectasis, aspiration, bacterial pneumonia, or contusion if applicable.
- Detection of granulomatous lesions from the donor should not be ignored as any endemic mycosis (e.g., *Coccidioides*, *Histoplasma*, *Blastomyces*, and *Paracoccidioides*) or even tuberculosis must be considered in the differential diagnosis.
- In cases where donors have central nervous system traumatic injury, bleeding and thrombotic events, or ventricular abnormalities and hydrocephalus, the symptoms of *Coccidioides* meningitis may not be considered even if the donor is at risk for this infection. Unexplained
altered mental status in donors from Coccidioides-endemic regions warrants a search for central nervous system Coccidioides infection.

- In Coccidioides-endemic regions, pre-transplant protocols should include assessment of epidemiological, occupational, and travel/residency information on prospective donors (and recipients) as these relate to coccidioidomycosis.

- In donors from endemic regions, suspicious lesions from lung or other sites (spleen, liver, renal, lymph nodes) should be rapidly screened by biopsy with pathologic examination, including looking for the presence of spherules or endospores.

- Donor Coccidioides serological screening should be attempted, especially from endemic regions. This is especially important in donor organs exported to centers outside endemic regions where personnel may be unfamiliar with coccidioidomycosis. Centers should be certain to communicate these results to the providers of the recipients.

Bernie Kubak, MD, PhD

Suggested reading:

1. VIKRAM H.R. AND BLAIR J.E. COCCIDIOIDOMYCOSIS IN TRANSPLANT RECIPIENTS: A PRIMER FOR CLINICIANS IN NONENDEMIC AREAS. CURR OPIN ORGAN TRANSPLANT. 2009;14(6):606-12


UPCOMING CHANGES TO DONOR HIV SCREENING TEST AVAILABILITY

As most OPOs know by now, the Abbott EIA HIVAB™ HIV-1/HIV-2 (rDNA) EIA (LN 3A77) will soon be retired. The product’s final lot expiration dating is reported to be March 2011. Is your OPO prepared for this change? OPTN Policy does not allow diagnostic testing of potential organ donors for anti-HIV. Please review the FDA’s Complete List of Donor Screening Assays for Infectious Agents and HIV Diagnostic Assays to make sure that your OPO is prepared for the change:

http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm080466.htm

REPORTING POST-TRANSPLANT TUMORS TO THE OPTN

Timely reporting to the Patient Safety System of tumors believed to be donor related provides the basis of an "early warning" system to notify those caring for other at-risk recipients when a suspected donor tumor transmission has been identified. This article highlights some things to consider when preparing to report a tumor that has been diagnosed in one of your patients.

Several different categories of tumors may arise in the organ or tissue recipient. In some cases, this may represent recurrence of a cancer that the patient had prior to transplant. In other cases de novo cancers may arise, similar to tumors that arise in non-transplant patients. Rarely, a cancer may be the result of inadvertent transmission of a tumor that was present in the donor at time of transplant. This last category of tumors calls for a more urgent approach to reporting, since there may be other recipients from the same donor, and these individuals may also be at increased risk for tumor development.
The question, of course, is when to suspect that a tumor may be of donor origin. No foolproof guidelines for true tumor origin exist short of molecular pathologic proof. However, some scenarios would raise reasonable suspicion of a possible donor-transmitted tumor, including:

1. Cancer (other than post-transplant lymphoproliferative disorder, PTLD) arising within the first 2 years after transplant.
2. Cancer arising in the allograft organ in a patient with no history of carcinoma in the corresponding native organ.
3. Metastatic carcinoma arising in an allograft recipient, particularly when a primary site cannot be identified.
4. Metastatic carcinoma of allograft type (e.g., renal cell carcinoma in a renal transplant patient) in a recipient with no known history of that type of cancer.
5. Central nervous system (CNS) neoplasm occurring outside of the CNS, particularly in a transplant patient with no known CNS involvement.
6. Sex-specific cancer (e.g., choriocarcinoma) arising in a transplant patient of the opposite sex.
7. Age discordant cancer (e.g., pediatric cancer arising in an adult transplant recipient, or vice versa).
8. Cancer in which there is specific suspicion of donor origin (e.g., use of organs from a donor with a known history of carcinoma).

Tumors arising in allograft organs a number of years after transplant may originate from allograft donor cells, but most likely did not exist as tumors at the time of transplant. But since we do not presently know the time interval beyond which other recipients from the same donor would no longer be at risk for possible tumor transmission, it is best to report all allograft-derived tumors (in patients without a history of cancer of the native organ) as potential donor transmitted tumors through both the Transplant Recipient Follow-up (TRF)/ Post-Transplant Malignancy (PTM) form AND the Patient Safety System until enough evidence is gathered to provide more specific guidance.

The approach to reporting post-transplant malignancies is straightforward:
1. All post-transplant PTLDs should be reported using the TRF/PTM forms only.
2. Per OPTN policy, tumors suspected of being of donor origin must be reported as a potential donor-derived disease transmission through the Patient Safety System portal (located in UNetSM) in addition to being reported using the TRF and PTM forms.
3. All other tumors (i.e. recurrent and de novo tumors not related to the donor) are reported using the TRF/PTM forms only.

Attention to the specific category of tumor arising in a transplant patient will aid you in correctly reporting this complication and thereby helping to serve our transplant patient population.

Michael Nalesnik, MD

A POTENTIAL DONOR-DERIVED DISEASE TRANSMISSION!
NOW WHAT?

Current OPTN policy requires members to report any event involving unexpected potential or proven transmission of a medical condition, including infections and malignancies, discovered after organ procurement to the OPTN Patient Safety System. The reporting portal is located on the front page of UNetSM. The DTAC will be creating a guidance document to help OPOs and transplant centers understand what should be reported. This document will go to the Board of Directors for approval in June 2011. In the interim, you may find it helpful to refer to this brief outline of what to expect when a case is reported as you become familiar with modifications to Policy 4.5 that will be implemented on January 10, 2011.

What do I report?
Your center should report when an organ recipient is suspected to have, is confirmed positive for, or has died from a potential transmissible disease or medical condition for which there is substantial concern that
it could be from donor origin.

If a Host OPO learns of new post-recovery information regarding a donor (i.e. final donor cultures, information from autopsy report, etc.) that was unknown prior to transplant that indicates risk of potential transmission of disease or malignancy to the organ recipient(s), this must be reported.

When in doubt it’s always best to report! A report can be reviewed by DTAC chair to determine whether the report meets policy requirements for reporting to begin case review. If you have questions regarding whether you have a reportable case, you may always contact an OPTN Patient Safety staff member:

<table>
<thead>
<tr>
<th>Name</th>
<th>Email</th>
<th>Phone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shandie Covington</td>
<td><a href="mailto:shandie.covington@unos.org">shandie.covington@unos.org</a></td>
<td>804-782-4929</td>
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<td>Kimberly Taylor</td>
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**When do I report?**
The transplant center that suspects potential transmission should not wait for all medical documentation that may eventually be available, but must inform the Host OPO and/or the OPTN Patient Safety System to transfer knowledge/concern as soon as possible to all centers that received organs from the donor in question.

The Host OPO must communicate test results and diagnosis from a suspected donor and/or affected recipients that may be pertinent to acute patient care as soon as practicable, not to exceed **24 hours** to all affected recipient transplant centers.

Prompt communication is key to promoting patient safety!

**Who do I communicate this information to outside of the OPTN Patient Safety System?**
OPOs and Transplant Centers are to develop a process for identifying a patient safety contact at their institution. This contact must be available 24 hours a day and is responsible for receiving this type of information and communicating it to the appropriate medical professional responsible for clinical care of the recipient(s) as soon as possible, and not to exceed 24 hours.

In many cases, this contact may be the coordinator on call for an OPO or transplant center, but the policy requirement was created to be flexible enough to allow members to develop a process that meets each organization’s specific needs. It is suggested that this information be shared at time of offer acceptance as a precaution.

**What happens after I report the event to the OPTN?**
When a potential disease transmission report is submitted through the Patient Safety System, a confirmatory email is received within an hour of submission. If you are the Host OPO, then you will also receive a copy of the Potential Disease Transmission Report (PDTR) Form (previously known as the Initial Report). This is to be completed and returned to OPTN Patient Safety staff within 24 hours.

The Host OPO is responsible for contacting each recipient center to notify the patient safety contact of the potential transmission event and record this contact information on the PDTR form.

OPTN Patient Safety staff will follow-up with all recipient centers (and the Host OPO as necessary) to collect additional information that the DTAC will review to classify the likelihood of donor-derived disease transmission. All information reviewed by DTAC is redacted to protect the confidential medical peer review process. Members may be asked to provide copies of follow-up testing or screening completed on the donor or recipient, information on plans for prophylaxis, treatment or long-term follow-up depending on the type of potentially transmitted disease or condition. You may be contacted by OPTN staff on more than one occasion during the course of the case review and you may be asked to complete a follow-up form to capture information regarding the recipients’ status. As the committee develops its classification of a case, this information will be shared with the OPO and transplant programs.
Potential malignancy transmissions may be followed beyond the traditional 45 day case review period. In all reported events, members are encouraged to contact OPTN Patient Safety staff if disease is noted in a recipient after completion of the 45 day case review.

**Why Do I Report Potential Transmission Events?**

Your participation is critical to promote patient safety and communication within the transplant community. The DTAC examines individual potential disease transmission cases reported to the OPTN in an effort to confirm transmissions where possible. It reviews aggregate data on all reported cases to assess the risk of donor disease transmission in organ transplantation in the U.S. with the goal of providing (1) education and guidance to the transplant community toward preventing future disease transmission and (2) input in developing policy to improve the safety of organ donation through the reduction of donor derived transmission events. It may identify disease-transmission related patient safety issues to be addressed, as appropriate, by the OPTN.

**COMING SOON TO THE DTAC NEWS…**

Everything you always wanted to know about donor derived infections but had no one to ask at 2 am during a donor evaluation. "What to do when it's 2 (am)".

This concept for addition to the DTAC Newsletter will give readers an opportunity to "ask the experts" questions about cases that you have been involved with, and had challenges answering issues related to potential transmission risks from donor to recipient. One to two questions based on real life cases will be selected from those submitted by OPO Medical Directors, Procurement Staff, Transplant Center Staff or other interested parties for commentary by the members of DTAC and answered in the next DTAC newsletter. Your participation is encouraged and appreciated!

Please send a brief, but pertinent, case synopsis with 2-3 questions to Dan Lebovitz, MD c/o Shandie Covington (shandie.covington@unos.org).

*Dan Lebovitz, MD*

**ADDITIONAL INFORMATION**

If you would have questions related to this newsletter, the DTAC, or you are interested in becoming a member of this committee, please contact Shandie Covington (OPTN/UNOS Staff Liaison to the DTAC) at shandie.covington@unos.org.