Guidance for Recognizing Central Nervous System Infections in Potential Deceased Organ Donors:
What to Consider During Donor Evaluation and Organ Offers

Summary and Goals

The Ad Hoc Disease Transmission Advisory Committee (DTAC) reviewed confirmed donor-derived disease transmission events involving both recognized and unrecognized central nervous system (CNS) infection in deceased organ donors reported from 2008 through 2011. Our review of reports submitted through the Improving Patient Safety portal in Secure EnterpriseSM indicates that CNS infection is not always recognized in donors, and has been associated with high rates of transmission to organ recipients with subsequent morbidity and mortality, as reflected in the attached abstract from Lyon et al presented at the 2011 American Transplant Congress. These events are of great concern due to the absence of effective treatments for most of these pathogens. Because recognition of these donors can be especially challenging, this guidance document has been developed to help identify donors at risk for transmission of pathogens associated with CNS infections.

To help OPOs and transplant centers better differentiate CNS infection from stroke in potential organ donors, the DTAC created a guidance document to outline indicators of possible meningoencephalitis in potential deceased organ donors. This information is meant to assist OPOs performing potential organ donor screening procedures and transplant center’s evaluation of organ offers from donors that may be suspected to have CNS infection.

This resource is not an OPTN policy, so it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, nor is it intended to be clinically prescriptive or to define a standard of care. This is a resource tool intended to be of educational support for OPOs and Transplant Centers and is for voluntary use by members.

Background

There are a number of types of CNS infections; however, undiagnosed meningoencephalitis (ME) poses the greatest risk to organ recipients. For the purposes of this document, ME is inflammation of both the brain and/or the membranes that surround it and can include meningitis and/or encephalitis. It can be caused by bacteria, viruses, fungi, or protozoa with case reports involving *Mycobacterium tuberculosis*, Lymphocytic choriomeningitis virus, West Nile Virus, Rabies, *Cryptococcus*, *Coccidioides immitis*, *Aspergillus*, and *Balamuthia*. With the exception of West Nile Virus, which is part of routine screening for tissue donors, none of these pathogens are part of the standard screening requirements for organ or tissue donors. Moreover, transmission can occur in the absence of clearly recognizable donor disease. In the majority of cases, diverse recipients have been affected, usually with adverse outcomes, including mortality and allograft loss. Although some of these events may be unavoidable due to the absence of donor symptoms, some transmissions have involved donors with CNS syndromes that were not initially attributed to infection. This guidance documents addresses such cases.

Recognizing Potential Meningoencephalitis

The clinical presentation and course in the donor with ME is not always clearly defined. A careful review of donor-derived disease ME transmissions reported to the OPTN does not
identify a conclusive set of risk factors associated with these infections. In most circumstances, organs from donors with diagnosed treatable forms of ME (e.g. pneumococcal meningitis) can be safely used if antimicrobial treatment is administered to both the donor and the recipient(s). In other cases, however, ME may be mistaken for a stroke and infection is not recognized or anticipated either through testing or medical-social history provided by friends or family of a potential donor. In this scenario, ME can lead to significant recipient morbidity and mortality.

**OPOs should consider the following questions when completing screening procedures for potential organ donors.** Transplant Programs should also be aware of these issues when considering organ offers.

- **What is the potential donor’s age and cause of brain death?** Were there any co-morbidities that may support stroke/CVA diagnosis (i.e. diabetes, hypertension, prior CVA) versus possible ME noted? Pediatric and young adult donors are less likely to have a stroke or CVA compared to older adults. Accordingly, caution should be used in evaluating younger potential donors given this diagnosis. While older adults being evaluated are more likely to have stroke/CVA diagnosis, atypical presentations and/or the absence of co-morbidities should prompt consideration for ME.

- **Did the potential donor have a fever at presentation of illness/admission?** (e.g. Fever defined as >37.5–38.3 °C (99.5–100.9 °F)? If yes, was there a clear explanation for this fever? If not, ME should be considered.

- **Were altered mental status and/or seizures part of the presentation that led to the donor’s hospitalization?** If these were new and/or unexplained events, ME may be considered.

- **Was a CT of the head, or MRI of the head or lumbar puncture consistent with an infectious process?** For example, was there an unexplained CSF pleocytosis, low CSF glucose, or elevated CSF protein without a clearly defined bacterial pathogen? Is there unexplained hydrocephalus - another potential indicator of CNS infection? Abnormal CSF due to clearly defined case of bacterial meningitis currently under treatment would be an exception. MRI may show a focal finding like infarct or hemorrhage; however, this may not necessarily exclude a diagnosis of ME.

- **Was the donor an immunosuppressed host?** This includes donors with a prior history of transplant on immunosuppressive medications (including steroids), a donor on immunosuppressive medications for other reasons, or with a history of an underlying condition associated with immunosuppression (i.e. cirrhosis, end stage renal disease, and other immune disorders).

- **Did the donor have any potential environmental exposures associated with organisms causing ME?** These exposures will vary depending on the region of the country and the time of year. For example, a donor with a recent bat exposure and mental status changes could have rabies. A donor who spent a lot of time outdoors in an area with heavy West Nile Virus activity would be at greater risk for WNV meningoencephalitis.
It should be noted that homeless donors or any donors in whom obtaining an adequate medical social history is problematic may pose a unique risk due to difficulty in collecting medical-social history and living conditions that may put them at increased risk for transmitting infection (e.g. tuberculosis or extended outdoor exposure that may increase risk for vector borne illness- like WNV, Lyme Disease, rabies, etc).

To summarize, all donors with fever (without another obvious cause) at or soon after presentation of illness and/or otherwise unexplained altered mental status should be considered for further evaluation to rule out ME.

- The potential donor should be discussed with the OPO’s Medical Director and, if possible, with Infectious Diseases and Neurology consultants.

- Consideration should be given to performing a lumbar puncture to look for evidence of ME, including non-bacterial pathogens. Additional testing based on geographic and/or demographic factors may be considered as these results may guide post-transplant recipient management if the organs are utilized.

If evidence suggests unsuspected or untreated CNS infection, caution should be considered in proceeding with allocation and acceptance of the organs for transplantation. Additionally, if ME is suspected and the suspected pathogen is one for which there are no treatment options (viral pathogens), extreme caution is urged before using any organs for transplantation. The risk must be balanced with risk of poor recipient outcome if this donor is not used. Appropriate information should accompany the informed consent process. Where relevant, issues relating to these concerns should be discussed with the potential recipients.

When to Report a Potential Donor-Derived Transmission Event

If the recipient is suspected to be at risk for disease transmission- either by the OPO or a transplant center, a potential donor-derived disease transmission event should be reported to the OPTN’s Improving Patient Safety portal per Policy 4.5. This promotes prompt intervention for other recipients of the same donor’s organs.
Infectious Disease Transmission from Organ Donors with Meningitis or Encephalitis


**Background:** Organ transplantation can be associated with transmission of infections. Meningoencephalitis (ME) has been under recognized in donors and has been associated with high rates of transmission to recipients with subsequent mortality.

**Methods:** For this abstract, ME is defined as meningitis or encephalitis. All reports to DTAC between January 1, 2008 and September 30, 2010 were searched for cases with: 1) a concern or diagnosis of ME in either the donor or a recipient, or 2) either the donor or any recipients had infection with an organism that could be associated with ME, e.g. tuberculosis, endemic fungi, West Nile virus (WNV), etc. Records were abstracted for clinical details.

**Results:** Of 386 reports to DTAC, 90 (23.3%) screened positive for potential ME. 13/386 (3.4%) had evidence of ME in the donor. Four (30.7%) of the 13 donors were noted to have ME pre-procurement of organs; none resulted in transmission. These 4 donors had *Streptococcus*, *Naegleria*, or presumed viral ME. There were 2 donors with bacterial ME where recipient antibiotics may have prevented infection and 2 with viral ME without transmission. In contrast, 5 donors with unrecognized ME resulted in 9 (69%) infections in 13 recipients. Of the 9 recipients, 7 (78%) developed ME, 3 of whom died, 1 developed disseminated cryptococcosis without ME, and 1 received antimicrobial intervention without evidence of disease. Of the 5 donors with ME, the listed causes of death at procurement were stroke/intracranial hemorrhage (3), acute demyelinating encephalomyelitis (1), and anoxia (1). The causes of unrecognized ME included *Balamuthia* (free-living ameba), *Cryptococcus*, and WNV. DTAC received reports of 9 (10%) recipients with ME caused by WNV, unknown etiology, toxoplasmosis, and amebiasis; none were donor derived.

**Conclusions:** Non-bacterial ME in the donor is highly associated with transmission to recipients and high morbidity and mortality. This study is limited because it is a passive reporting system, non-events are not reported. Potential organ donors who initially present with fever and an unexplained central nervous system event should be thoroughly evaluated for ME.