Diagnostic and Management Strategies for Donor-derived Infections

Pearlie P. Chong, MD*, Raymund R. Razonable, MD

KEYWORDS

- Donor-derived infections (DDIs) • Organ donor screening
- Potential donor-derived transmission events
- Organ procurement organizations (OPOs)
- Disease Transmission Advisory Committee
- United Network for Organ Sharing (UNOS)
- Organ Procurement and Transplantation Network (OPTN)

KEY POINTS

- Standard organ donor screening has not completely eliminated the risk of donor-derived infections (DDIs).
- The incidence of DDIs is thought to be rare, occurring in less than 1% of organ transplant recipients. It can, however, result in significant morbidity and mortality.
- Treating physicians need to maintain a high index of suspicion for DDIs in organ transplant recipients, especially if they occur during the early post-transplant period.
- Rapid recognition and prompt reporting of DDIs is crucial in enabling early institution of appropriate treatment and minimizing complications.
- Physicians who are involved in the management of organ transplant recipients should be familiar with the process of organ donor screening, as well as the process of reporting DDIs.

INTRODUCTION

Organ transplantation is a potentially life-saving procedure that has become standard of care for the management of numerous diseases. Each year, there are approximately 25,000 organ transplants performed across 250 transplant centers in the United States.[1] As graft survival rates have improved, due in part to better immunosuppression strategies, the number of transplant procedures performed continues to grow. To this end, evaluation of organ-donor suitability is an essential step in ensuring the safety of transplantation.

Funding Sources: None.
Conflict of Interest: None.
Division of Infectious Diseases, Department of Medicine, William J. von Liebig Transplant Center, College of Medicine, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905, USA
* Corresponding author.
E-mail address: Chong.Pearlie@mayo.edu

Infect Dis Clin N Am 27 (2013) 253–270
http://dx.doi.org/10.1016/j.idc.2013.02.001 **id.theclinics.com**
0891-5520/13/$ – see front matter Published by Elsevier Inc.

Standard organ donor screening, however, has not completely eliminated the risk of DDIs. Although a rare occurrence, such infections continue to occur, suggesting that there is room for improvement in the current approach to donor screening.[2] Standard screening procedures should be supplemented with specialized testing for donors with identifiable risks. For example, the spectrum of DDIs may be broad, to include parasitic infections such as Chagas disease and malaria, for recipients of organs from donors with diverse geographic exposures.

This article provides an overview of DDIs in solid organ transplant (SOT) recipients, focusing on approaches to diagnosis, prevention, and management strategies of these infections. Traditional DDIs, such as cytomegalovirus (CMV) and Epstein-Barr virus (EBV), are not discussed in this article.

INCIDENCE AND EPIDEMIOLOGY

The true incidence of DDIs is unknown. Current data suggest that potential donor-derived transmission events, including infections and malignancies, likely occur in less than 1% of transplant recipients.[3,4] This is likely an underestimation, however, of the true incidence due to under-recognition and under-reporting. This estimated rate also does not include expected DDIs, such as CMV and EBV. In spite of the rarity of DDIs, significant morbidity and mortality are associated with these events.[3,4] It is, therefore, crucial to consider the donor as the source of any post-transplant infections, especially if they occur during the first month after transplantation.[5]

CLASSIFICATION OF DONOR-DERIVED INFECTIONS AND THE REPORTING PROCESS

The Organ Procurement and Transplantation Network (OPTN), a private, nonprofit organization operated under contract with the US Department of Health and Human Services by the UNOS, establishes national standards to organ procurement and requires that all potential donor-derived transmission events be reported within 24 hours of knowledge or concern.[6] Treating physicians should have a logical approach to the work-up of potential DDIs and be aware that they have an obligation to report suspected and/or proven infections to the OPTN for further investigation. These events are reviewed by the Disease Transmission Advisory Committee (DTAC). DTAC is a web-based network established in 2005 to standardize the reporting and tracking process of donor-derived events, with the aim of decreasing transmission-associated morbidity and mortality. **Table 1** lists the potential DDI transmissions reported to the OPTN as of 2009.

In general, DDIs are classified as expected or unexpected.[7] Expected DDIs occur when routine pretransplant testing reveals donor infection and recipient susceptibility, but, because the benefits of transplantation outweigh the expected risks, this is considered acceptable medical practice. The most common example of expected DDIs is CMV infection transmitted from a CMV-seropositive donor to a CMV-seronegative recipient. Other examples of expected DDIs include EBV and toxoplasmosis.

On the contrary, unexpected DDIs are infections that are unrecognized until after transplantation has occurred. Although rare, these infections have often resulted in significant morbidity and/or mortality. Recent reports of transmission events include lymphocytic choriomeningitis virus (LCMV), rabies virus, West Nile virus (WNV), human immunodeficiency virus (HIV), hepatitis C virus (HCV), *Strongyloides stercoralis*, *Mycobacterium tuberculosis*, *Balamuthia mandrillaris*, and *Trypanosoma cruzi*.[7–16] A suspected event should further be classified as proven, probable, possible, or

Table 1
Potential donor-derived infectious diseases transmissions reported to the OPTN, 2005–2009

Disease	Number of Donor Reports	Number of Recipients with Confirmed Transmission	Number of DDD-Attributable Recipient Deaths
Virus	86	31	8
Bacteria	38	26	7
Fungus	30	26	8
Mycobacteria	26	10	2
Parasite	21	13	4
Total infections	201	106	29

Abbreviation: DDD, donor-derived infectious diseases.
Data from Ison MG, Nalesnik MA. An update on donor-derived disease transmission in organ transplantation. Am J Transplant 2011;11:1123–30.

excluded, according to the classification system developed by the Disease Transmission Advisory Committee in 2007.[3]

EVALUATION AND SCREENING OF POTENTIAL ORGAN DONORS

All organ donors (living and deceased) should be screened for medical conditions that may affect organ function, and for the presence of transmissible diseases and/or malignancies that may result in adverse outcomes in organ recipients. In the United States, the organ procurement organizations (OPOs) responding to an organ donor call from a hospital (called "Host OPO") is responsible for the process of identifying and evaluating potential organ donors as well as the process of organ procurement.[17]

Donor screening practices tend to vary among the various OPOs, but these programs are mandated by OPTN policy to subscribe to minimum requirements (**Box 1**). The host OPO should obtain a medical and behavioral history, focusing on the presence of risk factors for blood-borne pathogens, in particular HIV, hepatitis B

Box 1
Minimum procurement standards for an organ procurement organization (OPO)

1. Review of potential donor's medical and behavioral history
2. Pathogens for which potential donors must be routinely screened:
   - HIV
   - HBV
   - HCV
   - CMV
   - EBV
   - *Treponema pallidum* (syphilis)
3. Donors hospitalized $\geq$72 hours should have blood and urine cultures obtained.

Modified from 2004 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1994–2003. Department of Health and Human Services. Available at: http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy_2.pdf. Accessed October 11, 2012.

virus (HBV), and HCV (**Box 2**), in addition to the performance of specific screening serologic tests, as outlined in **Box 3**. Donors who meet exclusion criteria set forth by the US Public Health Service 1994 guidelines (**Box 4**) should generally be excluded from donation of organs and tissues. In special situations wherein such organs are considered for donation, informed consent should always be obtained from the potential recipient, and these should be documented in the medical records.

The threshold for acceptance of an organ for transplantation is not well established and continues to evolve as DDIs continue to be reported. In general, transplant teams and patients need to weigh the potential risk of disease transmission against the benefits of organ transplantation. For example, in febrile donors in whom the cause of fever is undefined, especially if encephalitis is present, physicians need to assess carefully if the risk of potential transmission of diseases, such as rabies, WNV, or LCMV, is acceptable. Generally, because of the lack of effective treatment and the potential fatal outcome of certain encephalitides, such as rabies and LCMV, the organs of such donors should be avoided.[18]

Laboratory Screening for Donor-derived Infections

In addition to review of medical history, laboratory screening for selected DDIs should be performed routinely (see **Box 3**). Serology and viral nucleic acid testing (NAT) are the 2 mainstays of laboratory testing of organ donors (discussed later).

Serologic testing

Serologic testing is an indirect method of disease detection because it relies on the ability of IgM and IgG production in response to antigen challenge. This forms the basis of humoral immune response because antigen-presenting cells stimulate immunoglobulin production by activated plasma cells. There is often a lapse between time of infection to production of disease-specific IgM and IgG, so-called "window period". Physicians should keep this in mind when interpreting serologic tests in the context of organ donor screening and diagnosis of DDIs.

Organ donors often require volume resuscitation, which leads to hemodilution and potentially false-negative serology results. All blood samples obtained from donors

Box 2
Suggested data to be collected regarding eligibility of organ donors

- Medical history
- Previous infections
- Occupational exposures
- Sexual behavior
- Incarceration
- Tattooing, ear piercing, or body piercing
- Use of illicit drugs
- Transfusions of blood or blood products
- Travel history
- Vaccinations
- Contact with bats, stray dogs, or rodents (including pets)

Data from Grossi PA, Fishman JA. Donor-derived infections in solid organ transplant recipients. Am J Transplant 2009;9(Suppl 4):S19–26.

Box 3
Standard screening tests for organ donors

- HIV antibody
- HBV serologies (including HBV surface antigen, core antibody, and surface antibody)
- Hepatitis delta antigen and/or antibody in hepatitis B surface antigen–positive donors
- HCV antibody
- Treponemal and nontreponemal testing (TP-HA, TP-PA, FTA-ABS and/or RPR)
- Toxoplasma antibody
- CMV antibody
- EBV antibody panel (EBV viral capsid antigen ± early antigen and nuclear antigen antibody levels)
- Herpes simplex virus antibody
- Varicella-zoster virus antibody
- Blood and urine cultures

Data from Grossi PA, Fishman JA. Donor-derived infections in solid organ transplant recipients. Am J Transplant 2009;9(Suppl 4):S19–26.

are currently required by the OPTN to be assessed for this phenomenon, using an FDA (Food and Drug Administration)–approved hemodilution calculation.[19] Thus, in situations where DDIs are strongly suspected with a suggestive clinical presentation but negative donor serologies, hemodilution should be considered a possible contributing factor. Alternatively, cross-reacting antibodies, newborns carrying maternal antibodies, and improperly performed tests may lead to false-positive serologic test results.

Viral nucleic acid testing

NAT involves the amplification of viral gene products and does not depend on host antibody response. Its major advantage is, therefore, its ability to detect the presence of an infection before antibody production, hence assisting in diagnosis during the window period.

In the United States, NAT has been routinely used to screen for HIV and HCV in blood donors since 1999.[20] It is however, not standard practice during organ donor screening.[21] Its role is currently limited to certain high-risk organ donors with specific behavioral risk factors (see **Box 2**), and OPOs are currently not mandated by the current OPTN policy to perform NAT testing. Recent highly publicized transplant-associated HIV and HCV transmission events have prompted further evaluation of incorporating NAT as part of routine organ donor screening. Using NAT may lead to earlier detection of HIV, HBV, and HCV.

Disadvantages of NAT include significant cost (because testing is performed for single-organ donors compared with batched testing in the blood or tissue donor populations); longer turnaround time, which may result in prolonged cold ischemia time and/or organ loss; increase in false-positive test results, which can lead to erroneous discarding of organs that could otherwise be potentially life saving; and lack of standardization. Some of the major limitations of NAT include the “eclipse period”, which is the time between infection to detection of viremia, leading to false-negative test results, and its inability to detect virus level below the lowest limit of detection of the assay. The perceived high sensitivity of NAT may lead to a false sense of security,

Box 4
Donor exclusion criteria

Behavior/history exclusionary criteria

1. Men who have had sex with another man in the preceding 5 years
2. Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years
3. Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates
4. Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years
5. Persons who have had sex in the preceding 12 months with any of the above person described in items 1–4 above or with a person known or suspected to have HIV infection
6. Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or mucous membrane
7. Inmates of correctional systems
8. Children born to mothers with HIV infection or mothers who meet the behavioral or laboratory exclusionary criteria for adult donors, unless HIV infection can be definitely excluded

Laboratory and other medical exclusionary criteria

1. Persons who cannot be tested for HIV infection because of refusal, inadequate blood samples (eg, hemodilution could result in false-negative tests), or any other reason
2. Persons with a repeatedly reactive screening assay for HIV-1 or HIV-2 antibody, regardless of the results of supplemental assays
3. Persons whose history, physical examination, medical records, or autopsy reports reveal other evidence of HIV infection or high-risk behavior, such as a diagnosis of AIDS, unexplained weight loss, night sweats, blue or purple spots on the skin or mucous membranes typical of Kaposi's sarcoma, unexplained lymphadenopathy lasting >1 month, unexplained temperature >100.5°F (38.6°C) for >10 days, unexplained persistent cough and shortness of breath, opportunistic infections, unexplained persistent diarrhea, male-to-male sexual contact, sexually transmitted diseases, or needle tracks or other signs of parenteral drug abuse

Modified from Guidelines for preventing transmission of human immunodeficiency virus through transplantation of human tissue and organs. Centers for Disease Control and Prevention. MMWR Recomm Rep 1994;43(RR-8):1–17. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/00031670.htm. Accessed October 11, 2012.

that a negative result translates into nontransmission. Recent transmission events of certain infections, such as LCMV and WNV, have been reported, in spite of negative NAT results, presumably due to the lack of significant viremia as these were performed in normal hosts.[22,23]

Living Donors

There are certain issues that pertain specifically to living donors. Living donors may acquire blood-borne viral infections, including HIV, HBV, and HCV, during the period between initial evaluation and transplant surgery. Thus, it is recommended that living donors be retested for these infections within 7 to 14 days of organ donation. This, however, is currently not uniformly practiced. A recent survey of New York State

transplant centers revealed that 3 months or more could have elapsed between a negative HIV enzyme immunoassay (EIA) result and time of transplant surgery.[24] Transplant centers should also routinely provide counseling to HIV-negative prospective living donors at the time of screening, specifically regarding approaches to decrease their risk for acquiring HIV, such as behavioral modification.

The Centers for Disease Control and Prevention (CDC) defines a high-risk donor as someone who carries an increased risk of harboring an infectious disease. The use of organs from high-risk donors is controversial and currently accounts for an average of 6.6% of all transplants, although this tends to vary among OPOs (0%–30%).[18] Specific recommendations for living high-risk donors include the consideration of delaying transplantation (until the time they are tested as negative) and using NAT rather than serologic testing where feasible to screen for blood-borne pathogens.

APPROACH TO RECIPIENT EVALUATION IN SUSPECTED DONOR-DERIVED INFECTIONS

Diagnosis of DDIs can be challenging for many reasons. Classic signs of infection are often absent, and patients may present with atypical syndromes. Due to their immunosuppressed states, diseases often disseminate early and progress rapidly. Often, the only clue may be the presence of disease in multiple recipients of organs from a common donor, and because organs procured from a donor are usually distributed across several institutions, this often leads to delay in disease recognition and treatment.

Treating physicians, therefore, need to maintain a high index of suspicion and think about the possibility of DDIs when faced with a patient who presents with atypical symptom complexes during the early post-transplant period. The local OPO should be contacted immediately, as soon as this is suspected. The OPO should then report the concern to the OPTN, as outlined previously. This eventually alerts the other centers to monitor their transplant recipients for the suspected disease.

SELECTED PATHOGEN-SPECIFIC DIAGNOSTIC AND MANAGEMENT STRATEGIES

Donor-derived Bacterial Infections

Bloodstream infection in organ donors

Organ donors often have risk factors that predispose them to developing bacterial infections. These risk factors include prolonged stay in ICUs; use of medical devices, (such as intravascular catheters, urinary catheters, and endotracheal intubation); and the presence of comorbidities. The OPTN requires that routine blood cultures be obtained from all organ donors hospitalized for at least 72 hours. Positive donor blood culture(s) is therefore not uncommon, although it is usually not recognized until after organ transplantation has occurred.

Historical cases have alerted clinicians to the potentially catastrophic consequences of bacterial transmission from donor to recipient, such as graft infections, arterial anastomotic disruption, poor initial graft function, and sepsis.[25] Recent data have not demonstrated these outcomes, however, and a review of 3 recent retrospective analyses showed zero transmission rates in such recipients.[25–27] It is likely that the modern practice of routine administration of broad-spectrum antimicrobials for perioperative prophylaxis has decreased the rate of bacterial transmission from organ donors, accounting for the lower reported incidence and clinical sequelae of transmission. Likewise, the prompt reporting of positive test results to transplant centers may have led to earlier institution of pathogen-directed treatment that might have averted adverse outcomes.

Management of SOT recipients with donor-derived bloodstream infections involves selection of pathogen-specific antimicrobial agents based on susceptibility results. The optimal duration of antimicrobial treatment is currently unknown, but in general, 7 to 10 days of pathogen-specific antimicrobial therapy is recommended for uncomplicated bloodstream infections.[25] Depending on the isolated pathogen, 14 days of therapy may be considered. In contrast to organ donors with uncomplicated bloodstream infections, current data does not support the use of organs from donors with severe sepsis and multiorgan failure, likely as a result of severe dysfunction in the lungs, heart, liver, and kidneys from these individuals with septic shock.[25]

Coagulase-negative staphylococci (and, if speciated, *Staphylococcus epidermidis*) and *Staphylococcus aureus*, represent some of the more commonly isolated microorganisms from donor blood cultures.[25–27] More recently, however, due to the increasing prevalence of multidrug-resistant organisms in ICUs, asymptomatic colonization and infection of organ donors have also become more common. Whether organs procured from such donors can be safely used remains actively debated. Although cultures are routinely obtained (from blood, urine, respiratory tract, and preservation fluid) at the time of transplantation, results are often not known until transplantation has occurred. This has resulted in poor outcomes, such as allograft loss and multiorgan failure with sepsis as well as death.[28,29] Therefore, some centers may opt not to use organs from donors infected with multidrug-resistant organisms. It seems that prior knowledge of donor infection and/or colonization with multidrug-resistant organisms and antibiotic susceptibility patterns may result in more favorable outcomes,[30] which is most likely due to early institution of appropriate antimicrobial prophylaxis and treatment.

Tuberculosis

Tuberculosis (TB) has an estimated incidence of 1.2% to 6.4% among SOT recipients in developed countries.[31] TB may be acquired via 1 of 3 ways: donor-derived, de novo acquisition from the community, or reactivation of recipient-derived latent infection. Although reactivation of latent TB is the most common cause of infection after transplantation, an estimated 4% of all TB infections in transplant recipients are thought to be donor derived.[8,32–34] When exposed to *Mycobacterium tuberculosis*, SOT recipients have a significantly higher risk of developing infection compared with the general population. In addition, the risk of dissemination and death due to TB is also higher.[35] Given the significant morbidity and mortality associated with post-transplant TB, organ donor and recipient screening should, therefore, be taken seriously.

A consensus report on the diagnosis and management of donor-derived TB was recently published (its recommendations are summarized later).[36] All living donors should undergo clinical evaluation for previously undiagnosed TB or latent TB infection (LTBI) in addition to either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) as part of routine donor screening process. Screening of deceased donors is, unfortunately, limited to identification of risk factors for TB by history and review of available medical records. In general, IGRAs and TSTs have comparable sensitivity in LTBI detection, except in those who have previously received Bacillus Calmette-Guérin vaccination, where IGRAs are preferred due to better specificity.[37] It was recently proposed that IGRAs may have a potential role in screening deceased donors for TB, but there are important limitations. A negative TST or IGRA should never be used to exclude active TB because 10% to 25% of those with active TB have negative TSTs (using a cutoff induration of 5 mm or greater), and the false-negative rate of TSTs in those with disseminated TB is approximately 50%.[38]

Diagnostic work-up of suspected cases should, therefore, routinely include acid-fast bacilli (AFB) staining and culture as well as nucleic acid amplification testing.

The risk of disease transmission in using organs from donors with a history of or active TB (including patients with LTBI) should be stratified into low to moderate or high-risk groups. Factors that should be taken into consideration during risk assessment include time of diagnosis and whether treatment completion was achieved and documented. In general, organs from donors with confirmed or possible active TB at the time of transplantation should not be used. Chemoprophylaxis with isoniazid should be considered and/or initiated in transplant recipients who received organs from donors with insufficiently treated LTBI. There are currently no data on the optimal timing for organ procurement from a living donor who is actively undergoing treatment of LTBI.

Treatment of active TB in SOT recipients is similar to that of the general population. A 4-drug regimen of isoniazid, a rifamycin, pyrazinamide, and ethambutol is used during the first 2 months pending susceptibility test results, followed by isoniazid and rifampin or rifabutin alone for an additional 4 months.[9] Longer duration of treatment should be considered the following situations: patients with central nervous system or bone and joint involvement; those with severe disseminated disease, as well as cavitary pulmonary disease with positive sputum culture at 2 months of treatment.[9]

Drug-drug interactions are a major challenge in the treatment of active TB in SOT recipients. Rifampin is an extremely potent inducer of cytochrome P3A4, leading to substantial decrease in serum levels of cyclosporine, tacrolimus, and sirolimus. Rejection episodes and subsequent allograft loss have been widely reported in conjunction with rifampin use. Because of the potent sterilizing activity of this drug class, a rifamycin-containing regimen remains strongly preferred. In this regard, rifabutin is a more attractive option, because it is a less potent inducer of cytochrome P3A4. Serum levels of the calcineurin inhibitors should be monitored closely, regardless of whether rifampin or rifabutin is used.

Donor-Derived Viral Infections

Rabies

Rabies is rare in the United States. Its incidence in the general population range from 2 to 6 cases per year.[10,11] Rabies virus transmission is predominantly neurotropic and occurs through bites and/or contact with neural tissue or saliva of infected animals. Transmission in the transplant population has occurred via corneal transplants and through organ and vessel segment transplantation.[39]

The onset of clinical signs and symptoms in SOT recipients occurred within the first 30 days of transplantation in reported cases, in contrast to the general population wherein only 25% of those infected tend to present within the first 30 days of exposure.[39] Although the incubation period seems shorter in SOT recipients, the tempo of disease progression seems similar in both patient populations. All 4 patients developed rapidly progressive encephalitis and died within 13 days of transplantation, similar to that in immunocompetent hosts.[39]

Diagnosis of rabies is challenging, especially in the absence of a documented exposure or suggestive history. Rabies virus serology (IgM and IgG antibodies) can be used for antemortem diagnosis confirmation. It seems that even in the setting of immunosuppression, seroconversion occurs: 3 of all 4 transplant recipients developed both IgM and IgG antibodies, and the other patient had only the IgG antibody to rabies virus.

There is currently no effective antiviral therapy for the treatment of rabies in humans.[40] The US Advisory Committee on Immunization Practices (ACIP) recommendations for

rabies postexposure prophylaxis do not contain specific guidelines for transplant recipients or immunosuppressed patients in general.[12,40,41]

Lymphocytic choriomeningitis virus (LCMV)

LCMV is a zoonosis caused by rodent-borne arenavirus. Transmission can occur either by direct contact with or aerosolization of secretions or excretions of infected rodents. As demonstrated by the 2003 and 2005 clusters reported in the literature, LCMV can be transmitted by transplantation.[22]

Infection in immunocompetent hosts is generally benign and rarely fatal. The spectrum of clinical manifestations in these patients ranges from asymptomatic infection to a mild, self-limited viral syndrome to aseptic meningitis. Data on the clinical manifestations and natural history of LCMV in immunocompromised patients are scarce. Immunosuppression is thought to lead to more severe clinical manifestations, because immune control of this viral infection requires cell-mediated immunity.[22,42]

There is currently no FDA-approved test to diagnose LCMV infection. Available assays are likely not sensitive enough to be used for routine organ donor screening purposes, as evidenced by the negative test results of these tests on clinical specimens obtained from the donors in both reported clusters. Immunohistochemical staining may be helpful in the early diagnosis of LCMV infection and frequently demonstrates necrotic and occasional hemorrhagic foci in tissues.[22] Viral inclusions and inflammation are however, frequently absent in the immunocompromised hosts.

Ribavirin has in vitro activity against LCMV but in vivo activity remains unproven.[43–45] Of the 8 SOT recipients in the 2 reported clusters of donor-derived LCMV infection, only 1 received ribavirin therapy and this patient is the only one who survived. Because this patient's immunosuppression was also considerably reduced, the specific contribution of ribavirin to clinical improvement remains unclear at this time.

West Nile virus

WNV infection is commonly acquired through mosquito bites. It can also be transmitted through blood transfusions and transplantation. Two clusters of organ transplant–associated WNV infection have been reported in the literature to date: in 2002, the organ donor had acquired WNV via blood transfusion,[23] whereas in the second report, in 2005, the organ donor was likely infected through mosquito bites, associated with outdoor exposure.[13] Routine screening of organ donors for WNV is currently neither required nor routinely performed in the United States, although the US blood supply has been routinely screened for WNV using NAT since 2003.[46]

The clinical manifestations of WNV infection in organ transplant recipients may vary from that of immunocompetent hosts in the following ways:

1. Higher likelihood of neuroinvasive disease (40 times the risk of the general population)
2. Cerebrospinal fluid (CSF) pleocytosis may be subtle or even absent
3. Prolonged incubation period with asymptomatic viremia

WNV serology and quantitative PCR can be helpful in the diagnosis of WNV infection. Serologic response to infections may be blunted due to underlying immunosuppression; therefore, a negative WNV serology (either serum or CSF) does not rule out the diagnosis. WNV PCR is probably more sensitive than serologic testing and, although not 100% sensitive, can be helpful in detection of asymptomatic viremia, especially if performed on specimens collected close to the time of organ recovery. Organ donors with positive WNV IgM and IgG antibodies but without detectable nucleic acid PCR, however, can still transmit WNV.

Treatment of WNV infection is supportive. Interferon, ribavirin, and intravenous immunoglobulin have not been proven to be effective.[47–49]

HIV

In the United States, screening organ donors for HIV infection has been a requirement since 1985.[50] Transmission of HIV through SOT is in general rare but does occur, suggesting that current screening protocols for HIV infection may be inadequate. The first documented case of HIV transmission in the United States from a living donor was reported in 2009, despite screening with serologic testing.[14] HIV screen by EIA performed in this donor 79 days before actual transplantation was negative. Retrospective HIV NAT testing on the donor's stored serum obtained 11 days pretransplant found a 98% phylogenetic match of the recipient's HIV strain.

This prompted a CDC-led survey of 18 kidney and liver New York State transplant centers to assess current HIV infection screening protocols for prospective living donors.[24] This study found a wide variation in evaluation practices among transplant centers, underscoring a need to standardize this screening process. Results from this survey and the reported case of HIV transmission led to revision of US Public Health Service guidelines (unpublished), which recommends retesting of living donors for blood-borne pathogens, in particular HIV, within 7 to 14 days of donation.

Donor-derived Fungal Infections

The incidence of donor-derived fungal infections is not known but estimated to be rare. Although not common, these infections can be associated with significant complications, such as fungal arteritis with or without mycotic aneurysms, anastomotic infections, fungus ball, and graft site abscesses.[51,52] Unrecognized fungal infections in organ donors at the time of transplantation and contamination of preservation fluid are common modalities of infection transmission. The Infectious Diseases Community of Practice of the American Society of Transplantation recently published guidelines addressing issues related to donor-derived fungal infections.[51]

Candidiasis

Kidney transplant recipients Donor-derived candidiasis is estimated to occur at a frequency of 1:1000 in kidney transplantation.[52] These infections can occur as a result of contamination of preservation fluid, rupture of abdominal viscus in the donor, or, in some cases, donor candidemia. There is evidence that contamination of preservation fluid is likely the main cause of donor-derived candidiasis, because isolates implicated have been genotypically linked to those recovered from the preservation fluid.[52] The predictive value of positive preservation fluid cultures for development of infection remains, however, undefined. Therefore, although few existing data are instructive for obtaining routine preservation fluid cultures at the time of organ transplantation, this practice is currently not mandated.

In the event that *Candida* species is visualized or grown in preservation fluid, or in cases where intestinal perforation was documented in an organ donor, the kidney recipient should undergo further microbiologic and radiographic testing, including obtaining cultures from blood, urine, and all other clinically relevant sites as well as renal allograft imaging with baseline and repeat Doppler ultrasound at 1 week. More detailed studies, such as CT or magnetic resonance angiography, should be considered in cases where the initial Doppler ultrasound is negative, because infection can be associated with various allograft vascular and anastomotic complications.[51]

While awaiting culture and imaging results, empiric antifungal therapy should be initiated, with the drug of choice being fluconazole. Although active against most

Candida species, polyenes are not regarded as first-line therapy due to nephrotoxicity. An echinocandin should be considered if there is high likelihood of non-albicans *Candida* and if lower urinary tract infection has been excluded (because it undergoes extensive metabolism and minimal urinary concentration).

Duration of antifungal therapy is determined by the presence or absence of infection. Antifungal therapy may be discontinued after 2 weeks if there is no clinical or microbiologic evidence of infection. Alternatively, patients with established infection may be treated for 4 to 6 weeks, with at least 6 weeks of treatment in patients with vascular involvement. Repeat imaging should be performed at the end of therapy.[51]

Nonkidney organ transplant recipients Routine antifungal prophylaxis is commonly used in lung transplant recipients.[53] Empiric antifungal therapy should be considered if donor respiratory samples yield *Candida* species, until bronchoscopic evaluation of anastomosis is performed. In patients with risk factors for anastomotic infection, a longer course of antifungal therapy should be considered.[54] Donor-derived candidiasis is unusual, however, after cardiac transplantation.[55]

In liver and pancreatic transplant recipients with visualization or growth of *candida* in preservation fluid, the management of these patients should follow that of kidney transplant recipients. Specifically pertaining to pancreatic transplantation, the act of opening or aspirating duodenal contents during the backbench procedure is associated with the development of *candida* arteritis post-transplantation.[56] This practice should, therefore, be discouraged.

Cryptococcosis

The majority of post-transplant cryptococcal infections are thought to represent reactivation of latent infection. Although relatively rare, transplant-associated cryptococcosis is well documented and should be considered in the following clinical scenarios:

1. Cryptococcosis documented at any site in the first 30 days after transplant
2. Demonstration of cryptococcus at the graft or surgical site
3. Diagnosis of cryptococcal disease in more than 1 recipient from a single donor

Donors with cryptococcal disease or involvement at any site can transmit infection.[57,58] Evaluation and management of SOT recipient diagnosed with cryptococcal disease is as outlined in the Infectious Diseases Society of America 2010 guidelines.[59] Diagnostic evaluation should include CSF analysis, serum and CSF cryptococcal antigen testing, and cultures of blood, urine, CSF, and all clinically infected sites. Patients with mild to moderate disease, in whom central nervous system disease has been excluded, may be treated with fluconazole alone. All other patients, including those with central nervous system or disseminated disease as well as those with moderate to severe pulmonary disease, should receive induction with combination therapy consisting of lipid formulation of amphotericin B and flucytosine for 14 days, followed by consolidation and maintenance with fluconazole. In general, treatment duration is 6 to 12 months. Immunosuppression should be reduced gradually to minimize the risk of immune reconstitution inflammatory syndrome, and physicians should be aware of drug-drug interactions between fluconazole and calcineurin inhibitors.[59]

Although cases of donor-derived *Cryptococcus gattii* have not been documented, the potential for its transmission exists, because *C. gattii* is known to infect individuals with and without identifiable immune defects. The diagnosis and treatment recommendations for *C. gattii* are the same as for *C. neoformans*.[59]

Aspergillus and other molds

Although *Aspergillus* species is the second most common cause of invasive fungal infections in SOT recipients, donor-derived invasive aspergillosis is overall rare.[60–62] Acquisition of unusual molds from contaminated water, such as *Apophysomyces elegans* (an agent of mucormycosis) and *Scedosporium apiospermum*, may occur in donors with specific epidemiologic risk factors, such as near-drowning victims.[63,64] These infections are associated with high rates of graft loss and a multitude of other complications similar to that associated with donor-derived candidiasis, as discussed previously. Diagnosis of invasive mold infections in SOT recipients continue to rely mainly on fungal cultures, as the use of antigen testing, such as galactomannan in this patient population is currently not well studied.

Coccidioidomycosis

Coccidioidomycosis occurs in 4% to 9% of transplant recipients in endemic areas.[65,66] It most commonly occurs during the first year post-transplantation. Although these cases often represent either reactivation of latent infection or *de novo* acquisition of disease, donor-derived coccidioidomycosis has also been described, with the majority of cases occurring in lung, and a few in kidney transplant recipients.[67–72]

All potential organ donors who currently reside or have resided or traveled to endemic areas should be screened for previous exposure to *Coccidioides* species by serologic testing. Universal screening, however, is not recommended for centers outside the endemic areas. Various serologic testing methods exist, and these include EIA, complement fixation, and immunodiffusion. The performance of these assays in transplant recipients have not been studied extensively, and false-negative results have been reported.[72]

Recipients of organs from a donor who is found to be seropositive or to have active infection should undergo clinical evaluation, baseline serologic testing, and prompt initiation of antifungal prophylaxis. Either fluconazole (400 mg daily) or itraconazole (200 mg twice daily) may be used, because both have been used and proved effective.[73,74] The optimal duration of antifungal prophylaxis has not been defined. Lifelong prophylaxis may be considered in lung transplant recipients because granulomas may harbor viable organisms. In non–lung organ transplant recipients, however, discontinuation of prophylaxis after 3 to 6 months may be considered with close monitoring for clinical or serologic evidence of coccidioidomycosis.

Patients with active disease should be treated according to the Infectious Diseases Society of America guidelines.[66] In general, fluconazole or itraconazole is the drug of choice, unless severe pneumonia or disseminated disease is present, in which case amphotericin B should be used initially. Treatment duration should be a minimum of 6 to 12 months, followed by lifelong antifungal prophylaxis once active coccidioidomycosis has been controlled to prevent relapse.[67]

Donor-derived Amoebic and Parasitic Infections

Donor-derived parasitic infections caused by *T cruzi*, *S stercoralis,* and *B mandrillaris* have recently emerged in transplant recipients in the United States.

Chagas disease

Donor-derived Chagas disease is an emerging infection in transplant recipients due to a steady increase of immigrants from Latin America and expansion of organ donor pool.[15,16] Data regarding seroprevalence of *T cruzi* among organ donors are limited but estimated to be approximately 0.25% to 1%.[75,76] Although universal organ donor screening is currently performed in areas with a high prevalence of at-risk individuals

(such as Los Angeles and Miami), current guidelines recommend a more targeted screening approach, using one of the FDA–approved or FDA–cleared EIAs or immunofluorescent assays in those who were either born or have resided in Mexico, Central America, or South America.[75]

Whether or not organs from seropositive donors should be used is controversial. Hearts from *T cruzi*–infected donors should be avoided, given the known tropism of this parasite.[77] Alternatively, the use of kidneys and/or livers from seropositive donors can be considered based on some data showing that not all transplants resulted in transmission of Chagas disease.[78,79] Informed consent, however, should be obtained, with close monitoring of transplant recipients, should a decision be made to use these organs. Recipient monitoring should rely primarily on direct detection of *T cruzi* either by PCR, Giemsa-stained peripheral blood smears, or microscopy of fresh buffy coat preparations. Frequency of laboratory monitoring should consist of weekly specimens for 2 months, every 2 weeks for the third month, and monthly thereafter from months 4 to 6 post-transplantation.[75]

Recipients with evidence of *T cruzi* infection should be treated with either benznidazole or nifurtimox, both of which are available for use under Investigational New Drug protocols from the CDC. Benznidazole is the preferred first-line drug in transplant recipients because it is better tolerated and has fewer potential drug interactions when compared to nifurtimox.[75]

SUMMARY

Organ donor screening remains an essential practice in risk reduction of disease transmission associated with organ transplantation. Some of the changes that may be in store in the future of screening for DDIs include multiplex NAT testing, which involves performance of multiple simultaneous assays on small blood samples, will hopefully improve efficiency and turnaround time as well as enforce post-transplant screening for HIV, HBV, and HCV in SOT recipients from high-risk donors as measures to improve patient outcomes. This risk, however, can never be entirely eliminated. Because not all disease transmission through transplantation can be prevented, rapid recognition is critical to facilitate appropriate treatment, minimize complications, and maintain public confidence in the safety of the process of organ transplantation.

REFERENCES

1. Grossi PA, Fishman JA. Donor-derived infections in solid organ transplant recipients. Am J Transplant 2009;9(Suppl 4):S19–26.
2. Humar A, Fishman JA. Donor-derived infection: old problem, new solutions? Am J Transplant 2008;8:1087–8.
3. Ison MG, Hager J, Blumberg E, et al. Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. Am J Transplant 2009;9(8):1929–35.
4. Ison MG, Nalesnik MA. An update on donor-derived disease transmission in organ transplantation. Am J Transplant 2011;11(6):1123–30.
5. Fishman JA. Infection in solid-organ transplant recipients. N Engl J Med 2007; 357(25):2601–14.
6. Minimum procurement standards for an organ procurement organization (OPO). Available at: http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy_2.pdf. Accessed August 24, 2012.

7. Morris MI, Fischer SA, Ison MG. Infections transmitted by transplantation. Infect Dis Clin North Am 2010;24:497–514.
8. Centers for Disease Control and Prevention (CDC). Transplantation-transmitted tuberculosis- Oklahoma and Texas, 2007. MMWR Morb Mortal Wkly Rep 2008; 57(13):333–6.
9. Subramaniam A, Dorman S. Mycobacterium tuberculosis in solid organ transplant recipients. Am J Transplant 2009;9(S4):S57–62.
10. Centers for Disease Control and Prevention (CDC). Human death associated with bat rabies- California, 2003. MMWR Morb Mortal Wkly Rep 2004;53(2):33–5.
11. Centers for Disease Control and Prevention (CDC). First human death associated with raccoon rabies – Virginia, 2003. MMWR Morb Mortal Wkly Rep 2003;52(45): 1102–3.
12. Rupprecht CE, Briggs D, Brown CM, et al, Centers for Disease Control and Prevention (CDC). Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies: recommendations of the advisory committee on immunization practices. MMWR Recomm Rep 2010;59(RR-2):1–9.
13. Centers for Disease Control and Prevention (CDC). West Nile virus infections in organ transplant recipients—New York and Pennsylvania, August-September, 2005. MMWR Morb Mortal Wkly Rep 2005;54(40):1021–3.
14. Centers for Disease Control and Prevention. HIV transmitted from a living organ donor- New York City, 2009. MMWR Morb Mortal Wkly Rep 2011;60(10):297–301.
15. Centers for Disease Control and Prevention (CDC). Chagas disease after organ transplantation- United States, 2001. MMWR Morb Mortal Wkly Rep 2002; 51(10):210–2.
16. Chagas disease after organ transplantation, Los Angeles, California, 2006. MMWR Morb Mortal Wkly Rep 2006;55(29):798–800.
17. OPTN/SRTR 2004 annual report. Richmond (VA): Organ Procurement and Transplantation Network, United Network for Organ Sharing; 2004. Available at: http://www.optn.org/data/annualReport.asp. Accessed August 24, 2012.
18. Kucirka LM, Singer AL, Segev DL. High infectious risk donors: what are the risks and when are they too high? Curr Opin Organ Transplant 2011;16(2):256–61.
19. Delmonico FL. Cadaver donor screening for infectious agents in solid organ transplantation. Clin Infect Dis 2000;31(3):781–6.
20. Stramer SL, Caglioti S, Strong DM. NAT of the United States and Canadian blood supply. Transfusion 2000;40(10):1165–8.
21. Humar A, Morris M, Blumberg E, et al. Nucleic acid testing (NAT) of organ donors: is the 'best' test the right test? A consensus conference report. Am J Transplant 2010;10:889–99.
22. Fischer SA, Graham MB, Kuehnert MJ, et al. Transmission of lymphocytic choriomeningitis virus by organ transplantation. N Engl J Med 2006;354:2235–49.
23. Iwamoto M, Jernigan DB, Guasch A, et al. Transmission of West Nile virus from an organ donor to four transplant recipients. N Engl J Med 2003;348:2196–203.
24. Kwan CK, Al-Samarrai T, Smith LC, et al. HIV screening practices for living organ donors, New York State, 2010: need for standard policies. Clin Infect Dis 2012; 55(7):990–5.
25. Lumbreras C, Sanz F, Gonzalez A, et al. Clinical significance of donor-unrecognized bacteremia in the outcome of solid-organ transplant recipients. Clin Infect Dis 2001;33:722–6.
26. Gonzalez-Segura C, Pascual M, Garcia Huete L, et al. Donors with positive blood culture: could they transmit infections to the recipients? Transplant Proc 2005;37: 3664–6.

27. Freeman R, Ioannis G, Falagas M, et al. Outcome of transplantation of organs procured from bacteremic donors. Transplantation 1999;68(8):1107–11.
28. Goldberg E, Bishara J, Lev S, et al. Organ transplantation from a donor colonized with a multidrug-resistant organism: a case report. Transpl Infect Dis 2012;14: 296–9.
29. Centers for Disease Control and Prevention (CDC). Transmission of multidrug-resistant escherichia coli through kidney transplantation—California and Texas 2009. MMWR Morb Mortal Wkly Rep 2010;59(50):1642–6.
30. Ariza-Heredia EJ, Patel R, Blumberg EA, et al. Outcomes of transplantation using organs from a donor infected with Klebsiella pneumoniae carbapenemase (KPC)-producing K. pneumoniae. Transpl Infect Dis 2012;14:229–36.
31. Munoz P, Rodriguez C, Bouza E. Mycobacterium tuberculosis infection in recipients of solid organ transplants. Clin Infect Dis 2005;40:581–7.
32. Peters TG, Reiter CG, Boswell RL. Transmission of tuberculosis by kidney transplantation. Transplantation 1984;38:514–6.
33. Ridgeway AL, Warner GS, Philips P, et al. Transmission of Mycobacterium tuberculosis to recipients of single lung transplants from the same donor. Am J Respir Crit Care Med 1996;153:1166–8.
34. Kiuchi T, Inomata Y, Uemoto S, et al. A hepatic graft tuberculosis transmitted from a living-related donor. Transplantation 1997;63:905–7.
35. Singh N, Paterson DL. Mycobacterium tuberculosis infection in solid organ transplant recipients: impact and implications for management. Clin Infect Dis 1998; 27:1266–77.
36. Morris MI, Daly JS, Blumberg E, et al. Diagnosis and management of tuberculosis in transplant donors: a donor-derived infections consensus conference report. Am J Transplant 2012;12:2288–300.
37. Pai M, Zwerling A, Menzies D. Systematic review: T-cell based assays for the diagnosis of latent tuberculosis infection: an update. Ann Intern Med 2008;149: 177–84.
38. Sester M, Sotgiu G, Lange C, et al. Interferon-gamma release assays for the diagnosis of active tuberculosis: a systematic review and meta-analysis. Eur Respir J 2011;37:100–11.
39. Srinivasan A, Burton EC, Kuehnert MJ, et al. Transmission of rabies virus from an organ donor to four transplant recipients. N Engl J Med 2005;352:1103–11.
40. Gibbons RV, Rupprecht CE. Postexposure rabies prophylaxis in immunosuppressed patients. JAMA 2001;285(12):1574.
41. Hay E, Derazon H, Bukish N, et al. Postexposure rabies prophylaxis in a patient with lymphoma. JAMA 2001;285(2):166–7.
42. Amman BR, Pavlin BI, Albarino CG, et al. Pet rodents and fatal lymphocytic choriomeningitis in transplant patients. Emerg Infect Dis 2007;13(5):719–25.
43. Moreno H, Gallego I, Sevilla N, et al. Ribavirin can be mutagenic for arenaviruses. J Virol 2011;85(14):7246–55.
44. Enria DA, Maiztegi JI. Antiviral treatment of Argentine hemorrhagic fever. Antiviral Res 1994;23:23–31.
45. Moreno H, Grande-Perez A, Domingo E, et al. Arenaviruses and lethal mutagenesis: prospects for new ribavirin-based interventions. Viruses 2012;4(11): 2786–805.
46. Busch MP, Caglioti S, Robertson E, et al. Screening the blood supply for West Nile virus RNA by nucleic acid amplification testing. N Engl J Med 2005;353:460–7.
47. Gea-Banacloche J, Johnson RT, Bagic A, et al. West Nile virus: pathogenesis and therapeutic options. Ann Intern Med 2004;140:545–53.

48. Planitzer GB, Modrof J, Kreil TR, et al. West Nile virus neutralization by US plasma-derived immunoglobulin products. J Infect Dis 2007;196(3):435.
49. Agrawal AG, Petersen LR. Human immunoglobulin as treatment for WNV infection. J Infect Dis 2003;188(1):1.
50. Rogers MF, Simonds RJ, Lawton KE, et al. Guidelines for preventing transmission of human immunodeficiency virus through transplantation of human tissue and organs. Centers for Disease Control and Prevention. MMWR Recomm Rep 1994; 43(RR-9):1–17.
51. Singh N, Huprikar S, Burdette SD, et al. Donor-derived fungal infections in organ transplant recipients: guidelines of the American Society of Transplantation, Infectious Diseases Community of Practice. Am J Transplant 2012;12:2414–28.
52. Albano L, Bretagne S, Mamzer-Bruneel MF, et al. Evidence that graft-site candidiasis after kidney transplantation is acquired during organ recovery: a multicenter study in France. Clin Infect Dis 2009;48:194–202.
53. Dummer JS, Lazariashvilli N, Barnes J, et al. A survey of antifungal management in lung transplantation. J Heart Lung Transplant 2004;12:1376–81.
54. Hadjiliadis DH, Howell DN, Davis RD, et al. Anastomotic infections in lung transplant recipients. Ann Transplant 2000;3:13–9.
55. Mossad SB, Avery RK, Goormastic M, et al. Significance of positive cultures from donor left atrium and post-preservation fluid in heart transplantation. Transplantation 1997;64:1209–10.
56. Ciancio G, Brke GW, Viciana AL, et al. Destructive allograft fungal arteritis following simultaneous pancreas-kidney transplantation. Transplantation 1996; 61:1172–5.
57. Baddley JW, Schain DC, Gupte AA, et al. Transmission of cryptococcus neoformans by organ transplantation. Clin Infect Dis 2011;52:e94–8.
58. Sun HY, Alexander BD, Lortholary O, et al. Unrecognized pretransplant and donor-derived cryptococcal disease in organ transplant recipients. Clin Infect Dis 2010;51:1062–9.
59. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of America. Clin Infect Dis 2010;50:291–322.
60. Keating MR, Guerrero MA, Daly RC, et al. Transmission of invasive aspergillosis from a subclinically infected donor to three different organ transplant recipients. Chest 1996;109:1119–24.
61. Mueller NJ, Weisser M, Fehr T, et al. Donor-derived aspergillosis from use of a solid organ recipient as a multiorgan donor. Transpl Infect Dis 2010;12:54–9.
62. Shoham S, Hinestrosa F, Moore J, et al. Invasive filamentous fungal infections associated with renal transplant tourism. Transpl Infect Dis 2010;12:371–4.
63. Stas KJ, Louwagie PG, Van Damme BJ, et al. Isolated zygomycosis in a bought living unrelated renal transplant. Transpl Int 1996;9:600–2.
64. Rammaert B, Lanternier F, Zahar JR, et al. Healthcare-associated mucormycosis. Clin Infect Dis 2012;54(Suppl 1):S44.
65. Blair JE, Logan JL. Coccidioidomycosis in solid organ transplantation. Clin Infect Dis 2001;33:1536–44.
66. Galgiani JN, Ampel NM, Blair JE, et al. IDSA guidelines: coccidioidomycosis. Clin Infect Dis 2005;41:1217–23.
67. Miller M, Hendren R, Gilligan P. Posttransplantation disseminated coccidioidomycosiss acquired from donor lungs. J Clin Microbiol 2004;42:2347–9.
68. Tripathy U, yung GL, Kriett JM, et al. Donor transfer of pulmonary coccidioidomycosis in lung transplantation. Ann Thorac Surg 2002;73:306–8.

69. Brugiere O, Forget E, Biondi G, et al. Coccidioidomycosis in a lung transplant recipient acquired from the donor graft in France. Transplantation 2009;88: 1319–20.
70. Vikram HR, Dosanjh A, Blair JE. Coccidioidomycosis and lung transplantation. Transplantation 2011;92:717–21.
71. Carvalho C, Ferreira I, Gaiao S, et al. Cerebral coccidioidomycosis after renal transplantation in a non-endemic area. Transpl Infect Dis 2010;12:151–4.
72. Proia L, Miller R, AST Infectious Diseases Community of Practice. Endemic fungal infections in solid organ transplant recipients. Am J Transplant 2009;9(Suppl 4): S199–207.
73. Blair JE, Douglas DD, Mulligan DC. Early results of targeted prophylaxis for coccidioidomycosis in patients undergoing orthotopic liver transplantation within an endemic area. Transpl Infect Dis 2003;5:3–8.
74. Blair J, Braddy C. Azoles prevent reactivation of prior and clinically quiescent coccidioidomycosis in patients undergoing solid organ transplantation. Presented at the 45th annual Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington, DC, December 16–19, 2005.
75. Chin-Hong PV, Schwartz BS, Bem C, et al. Screening and treatment of chagas disease in organ transplant recipients in the United States: recommendations from the Chagas in Transplant Working Group. Am J Transplant 2011;11:672–80.
76. Nowicki MJ, Chinchilla C, Corado L, et al. Prevalence of antibodies to Trypanosoma cruzi among solid organ donors in Southern California: a population at risk. Transplantation 2008;81:477–9.
77. Kun H, Moore A, Mascola L, et al. Transmission of Trypanosoma cruzi by heart transplantation. Clin Infect Dis 2009;48:1534–40.
78. Riarte A, Luna C, Sabatiello R, et al. Chagas' disease in patients with kidney transplants: 7 years of experience 1989-1996. Clin Infect Dis 1999;29:561–7.
79. De Artega J, Massari PU, Galli B, et al. Renal Transplantation and Chagas' disease. Transplant Proc 1992;24:1900–1.