Screening of donor and recipient prior to solid organ transplantation

Background

Pre-transplant screening of potential organ donors and recipients is an essential part of solid organ transplantation. The goals of pretransplant infectious disease screening are: (1) to identify conditions which disqualify either donor or recipient, (2) to identify and treat active infection pretransplant, (3) to define the level of infection risk in order to determine strategies for preventing post-transplant infection. Although there is general agreement on the major infections for which screening is performed, there is some variation between centers in types of screening utilized and actions taken as a result.

The pretransplant period is an ideal time for detailed counseling of the recipient regarding food and other infection risks, as well as for obtaining a thorough travel, animal, and environmental exposure history. Given all of the events occurring before and after listing for transplant, patients and families may be overwhelmed, and it may be necessary to impart information over the course of several sessions. This will aid in reinforcing information and updating the patient regarding newer risks and recommendations. It is an important time for updating immunizations as well, since these will often be more effective when administered prior to transplant.

A large variety of pathogens may be transmitted by transplantation (1,2). Guidelines for pretransplant screening have been the subject of several recent publications (3–7) including a consensus conference of the Immunocompromised Host Society (ICHS) (3,4) the American Society for Transplantation (AST) Clinical Practice Guidelines on the evaluation of renal transplant candidates (8), and the ASTP Clinical Practice Guidelines on the evaluation of living renal transplant donors (9). Updated recommendations regarding hepatitis status of the donor have been summarized in the March 2001 Crystal City Meeting (10) and in a review by Chung, Feng, and Delmonico (11). In addition, the Centers for Disease Control and Prevention (CDC), the Infectious Disease Society of America (IDSA) and the American Society for Blood and Marrow Transplantation (ASBMT) have published guidelines for prevention of infection in hematopoietic stem cell transplant recipients (12), and the CDC has published guidelines for the prevention of HIV transmission through transplantation (13).

After a brief discussion of the differences in screening between living and deceased donors, this review will summarize current opinion on screening for bacterial, mycobacterial, fungal, parasitic, and viral infections in the donor and recipient. More detailed discussions of these infections and corresponding post-transplant monitoring and prophylaxis will be found in other sections of these guidelines. Because the viral serologies of donor and recipient are so closely tied together, these will be discussed together.

Given the limited pool of donors, it has become increasingly important to consider marginal candidates, including those with infection at the time of donation. The nature of this infection and the severity of recipient illness are important considerations when determining the acceptability of the infected donor.

Donor screening: living donor vs. deceased donor

The differences in screening of the living donor and the deceased donor are largely based on the different time frames during which this screening takes place. For the living donor, it is possible to treat active infection and to defer the transplant until after such infection resolves. Living donor screening is conducted at the transplant center. The time between screening and transplantation is variable, especially with altruistic donors for whom some programs require reflection periods of greater than 2 months. Clinical events occurring in the interim are taken into account at the time of transplantation. Repeat serologic testing should be considered in the presence of behavioral changes or appropriate clinical symptoms or signs, particularly any febrile or flu-like illness between the time of initial screening and transplantation.

The screening of a prospective living donor includes a thorough medical history and physical examination, laboratory studies including serologic testing (Table 1) and radiographic studies as needed. The medical history should include previous infections, vaccinations, travel and occupational exposures, as well as assessing for the presence of risky behaviors (drug use, sexual practices, incarceration). Living donors should be screened for untreated syphilis and a PPD skin test should be performed (see below).

By contrast, the time frame for deceased donor evaluation is typically hours. The laboratories associated with organ
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Table 1: Frequently utilized serologic tests for screening of donor and recipient prior to transplantation

| Tests Commonly Obtained in Both Donor and Recipient |
|----------------------------------------------------|
| Human immunodeficiency virus (HIV) antibody (HIV-1 and HIV-2 commonly obtained) |
| Human T cell lymphotropic virus (HTLV)-I/II antibody |
| HSV (herpes simplex) IgG antibody (at some centers) |
| Cytomegalovirus (CMV) IgG antibody |
| Hepatitis C (HCV) antibody |
| Hepatitis B (HBV) surface antigen (HBsAg) |
| Hepatitis B core antibody (HBcAb IgM and IgG) |
| Hepatitis B surface antibody (HBsAb) at some centers |
| Rapid plasma reagin (RPR) |
| Toxoplasma antibody (especially in heart recipients) |
| Epstein-Barr virus (EBV) antibody panel* |
| Varicella-zoster virus (VZV) antibody* |

Other Screening Measures for Infectious Diseases

- PPD skin testing (all candidates, preferably with anergy panel)
- Strongyloides serology, consider use of stool ova and parasites for candidates from endemic areas
- Coccidioides serology (for candidates from endemic areas)
- Trypanosoma cruzi serology (for donors and recipients from endemic areas)
- West Nile virus (note recent recommendation for NAT testing of live donors, see text)
- HHV-8 (KSHV)
- HHV-6 (in pediatric transplantation)*

*Particularly important in pediatric transplant candidates who are much more likely to be seronegative

Table 2: Interventions related to donor screening results

| Serologic finding | Action |
|-------------------|--------|
| Antibody to HIV | Exclude from organ donation |
| Antibody to HTLV VII | Generally exclude from organ donation (may be used in life-threatening situations, with informed consent) |
| Antibody to HCV | If used, usually reserve organ for recipient with antibody to HCV or severely ill recipient |
| Antibody to CMV | Use information to determine prophylaxis (in conjunction with recipient serology) |
| Antibody to EBV | Consider PCR monitoring if donor seropositive, recipient seronegative |
| Hepatitis B surface antigen (HBsAg+) or HBcAb IgM+ | Exclude from organ donation (possible use in life-threatening situations with intensive prophylaxis (11)) |
| Hepatitis B core antibody IgG (HBcAb IgG +) | Generally safe for organ donation |
| Hepatitis B surface antibody (HBsAb +) | High-risk for transmission if liver used for donation, but used at some centers with intensive prophylaxis; nonhepatic organs carry a small risk of transmission of HBV and are used for vaccinated recipients or with prophylaxis (11) |
| RPR+ | Not a contraindication to donation. Recipient should receive benzathine penicillin |
| Antibody to Toxoplasma | Not a contraindication to donation. Sulfadiazine prophylaxis recipients with a seropositive donor should receive pyrimethamine prophylaxis |

procurement organizations (OPOs) operate on a 24-h basis to generate the information needed to determine donor suitability (3,5,6). Because of the short time frame, there is a possibility that certain infections, such as HIV or HCV, may be present at an early stage, prior to the development of specific antibody (14). Thus, considerable weight is placed on the donor’s social and medical history in identifying potential risks that might not be reflected in serologic testing (13). Furthermore, certain infections (e.g. donor bacteremia) may come to light only after the transplant has been performed (15,16). In the future, rapid molecular testing may grant OPOs the capability for immediate detection, particularly of viral infections such as HCV and HIV.

**Donor screening: bacterial infections**

The evaluation detailed above will reveal most active bacterial infections present in the living donor. Infections of the respiratory tract, urinary tract, or other focal sites should be thoroughly treated and resolution of such infection should be documented. Particular caution must be employed if a urinary tract infection has occurred in a potential kidney donor, to make sure that this does not represent occult upper tract infection. If any illness has occurred which might have involved bacteremia, a thorough investigation should be performed to make sure that the target organ has not been seeded.
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Syphilis may be latent and asymptomatic and requires therapy if time permits; however, syphilis has rarely been transmitted by transplantation and is not a contraindication to organ donation if the recipient is treated posttransplant with an appropriate course of benzathine penicillin (17,18) (AII).

Deceased donors may harbor known or unsuspected bacterial infections and should be rapidly evaluated for these by review of medical records, temperature chart, radiography, and cultures when available. Organs that are known to be infected should not be transplanted (19,20) (AII). It is desirable to obtain blood cultures since occult donor bacteremia may occur. In addition to the risk of sepsis, well-documented cases have occurred of mycotic aneurysms at vascular anastomoses in the recipient, due to donor bacteremia with virulent organisms such as *Staphylococcus aureus* and *Pseudomonas* (2,21,22). Although a recent review of 95 bacteremic donors found no evidence of transmission when recipients were given antimicrobial therapy for a mean of 3.8 days posttransplant (15), it is prudent to employ longer courses of therapy (e.g. 2–4 weeks) if donors are known to have been bacteremic with potentially virulent organisms (2) (BIII).

In general, there is no compelling evidence to support treating a recipient who receives an allograft from a deceased donor with nonbacteremic, localized infection not involving the transplanted organ, with the exception of meningitis (CIII). Organs have been successfully transplanted from donors with bacterial meningitis with no evidence of infectious complications in the recipients, when appropriate antimicrobial therapy was administered to both donors and recipients (23,24).

Donor lung colonization in the case of lung transplantation deserves special attention. Donor bacterial colonization is extremely common given that the lungs are in contact with the external environment. Donor bronchoscopy with cultures, performed at the time of lung transplantation, allows for administration of antibiotics directed at these colonizing organisms, thus preventing invasive infection in the recipient (AII).

*Allograft contamination* may occur during procurement or processing (19,25). Rubin recommends administration of antibiotics to the recipient if organisms are isolated in perfusates or organ transplant medium (2), again citing the risk of mycotic aneurysm formation as discussed above. Antibiotics should be given for at least 14 days for Gram-negative bacilli, *Staphylococcus aureus*, or *Candida* species (2) (BIII). A shorter course of therapy may be considered for less virulent organisms (CIII). Although one study of donor left atrial cultures and preservation fluid cultures showed no correlation between these cultures and infection in heart transplant recipients, some recipients had received directed antibiotic therapy (16).

**Donor screening: mycobacterial infections**

*Mycobacterium tuberculosis* has been transmitted by transplantation (27,28); donor transmission accounted for approximately 4% of reported post-transplant TB cases in the large review of 511 patients by Singh and Paterson (28). Potential living donors should have a PPD (tuberculin skin test) performed, and if positive, should undergo additional screening to rule out active disease (AII). If there are abnormalities on chest X-ray or any symptoms suggestive of possible active disease, sputum AFB cultures should be performed, and chest CT is helpful. Urine AFB cultures are often obtained in the case of a PPD-positive prospective kidney donor, and radiography performed during donor pretransplant evaluation will often provide clues to present or past tuberculosis disease in the urinary tract. If there are no signs or symptoms of active disease and the chest X-ray is normal, sputum AFB cultures are very low-yield.

Although the time frame for evaluation of deceased donors does not allow for tuberculin skin testing, donors in whom active tuberculosis is a clinical possibility should not be utilized (AII).

Donors with a positive PPD but without evidence of active disease may donate organs even if they have never received prophylaxis. Donor PPD positivity without prior therapy is listed as an indication for isoniazid prophylaxis of the recipient in the review by Singh and Paterson (28) (BIII). In the past, the decision whether or not to prophylaxe a recipient who receives an allograft from a deceased donor with nonbacteremic, localized infection not involving a recipient who receives an allograft from a deceased donor who has meningitis is not traditionally been considered a contraindication to donation (BIII). Transmission of coccidioidomycosis by lung transplantation has been reported in the South-western USA (31), although reactivation of coccidioidomycosis in the recipient appears to be far more common (32). As yet, uniform recommendations for donor screening for endemic mycoses have not emerged.
**Donor screening: parasitic infections**

Toxoplasmosis is a major concern particularly in heart transplantation, where the *Toxoplasma*-seronegative recipient of a *Toxoplasma*-seropositive heart is at highest risk for developing active toxoplasmosis post-transplant (33). Toxoplasmosis has also rarely been transmitted to liver (34) and kidney (35) recipients. Knowledge of donor seropositivity does not contraindicate heart donation but does allow for appropriate prophylaxis to be administered (36). Screening of donors for *Toxoplasma* is not routinely performed for noncardiac donors.

Transmission of Chagas’ disease (*Trypanosoma cruzi*) by transplantation is a significant problem in endemic areas (South and Latin America) but has only recently been reported in the USA (37). Routine screening is not yet mandated in the USA, but if the prospective donor has resided in an endemic area, it is advisable (AIII). (Further discussion of these issues is found in the Parasitology section of these guidelines.)

**Donor and recipient screening: viral infections – CMV**

The following sections will discuss both donor and recipient screening for viral infections since the combined donor and recipient serologies are often crucial in determining risk of infection. All of the viral infections mentioned here are discussed in more detail in other sections of these guidelines. The CMV serologic status of donor and recipient is an important predictor of post-transplant events (38), with the CMV seronegative recipient of a CMV seropositive donor organ (D+/R–) being at highest risk for development of tissue-invasive CMV (2), recurrent CMV (39), and ganciclovir-resistant CMV (40). However, D+/R– status is not generally considered a contraindication to transplantation, but is an indication for more intensive monitoring and prevention strategies posttransplant (AI). The seropositive recipient, regardless of donor status, is also at risk for CMV and usually receives either prophylaxis or pre-emptive monitoring. There are many different protocols in use (41); a full discussion of CMV prevention is found in another section.

**Donor and recipient screening: viral infections – EBV**

Posttransplant lymphoproliferative disease (PTLD) is a feared complication of transplantation. The highest PTLD risk is in the EBV seronegative recipient of an EBV seropositive graft (42), which most commonly occurs in pediatric recipients but can occasionally occur in adults. PTLD can also develop in the seropositive recipient under the influence of augmented immunosuppression (42). Awareness of pretransplant serologies can target the highest risk group for close monitoring by EBV-PCR (43) and preemptive therapy (44) posttransplant (AI). Centers performing pediatric transplantation should consider adding EBV serology to their donor and recipient serologic panel if not already doing so (AI).

**Donor and recipient screening: viral infections – other herpesviruses**

Other herpesviruses of clinical importance in the transplant recipient include herpes simplex virus (HSV-1 and HSV-2), varicella-zoster virus (VZV), human herpesvirus-6 and 7 (HHV-6 and 7), and HHV-8 (KSHV). HSV screening is performed by some centers, whereas other centers administer universal antiviral prophylaxis during at least the first month post-transplant. VZV screening of the recipient is extremely important in that the varicella vaccine should ideally be administered pretransplant to seronegative recipients, to prevent severe primary varicella from occurring after transplant (45) (AI). In addition, knowledge of VZV serostatus after transplant is important in the management of VZV exposures.

Recent awareness of the possible roles of the roseoloviruses HHV-6 and HHV-7 as cofactors for CMV effects (46), fungal infections (47), and possibly allograft dysfunction has led to increasing interest in these viruses. Since almost all adults are seropositive, however, donor and recipient screening for these viruses has not generally been recommended. Whether or not such screening would be helpful in pediatric transplant programs is as yet unknown. HHV-8, the agent of Kaposi’s sarcoma, can reactivate after transplantation and occasionally may be transmitted by transplantation (48-50); it may also be associated with EBV-negative lymphoproliferative disease (51). Optimal strategies for prevention of reactivation have not been defined, and recommendations for pretransplant screening have yet to emerge (CIII).

**Donor and recipient screening: viral infections – HBV**

The issues surrounding HBV and transplantation are discussed in more detail in the hepatitis section of these guidelines. Donor screening usually includes at least HBsAg and HBV core antibody (HBcAb, most useful when performed as IgG and IgM). Donor HBsAg positivity or HBcAb-IgM positivity indicates active HBV infection (HBsAg negative, HBcAb-IgM positive persons may be in the ‘window period’) and such donors have generally not been utilized, although some centers have used these donors with intensive post-transplant prophylaxis (11). Isolated HBsAb positivity usually indicates prior vaccination or resolved infection and is not generally considered a risk for HBV transmission.

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The most complex question is the use of the HBsAg negative, HBcAb-IgG positive donor (11). This may represent either a false-positive test (if isolated HBcAb positive), or prior, latent HBV infection. If the latter, there is a significant risk of transmission of HBV to a liver transplant recipient (52), and therefore these livers are often not utilized (DII); however, some centers have successfully utilized livers from HBcAb positive donors with intensive posttransplant prophylaxis (11,53). The risk for transmission to nonhepatic recipients appears to be low but not zero; this risk can be further diminished by pretransplant HBV vaccination of the recipient (2,11,52,54). Some centers restrict the use of such organs to life-threatening situations and/or vaccinated recipients, or would utilize posttransplant prophylaxis with hepatitis B immune globulin (HBIg) and/or lamivudine if transplanted into a nonimmune recipient (BII) (11). Because of the possibility of being offered such an organ, it is prudent to vaccinate all seronegative transplant candidates with HBV vaccine, although the response to this vaccine in patients with end-stage organ disease may be suboptimal (55) (AII). A donor HBV-DNA level provides helpful information for designing prophylactic strategies, even if the result is received after transplant. Detailed recommendations for posttransplant prophylaxis can be found in Chung et al. (11), and in the HBV section of these guidelines.

Recipient screening for HBV is helpful in posttransplant management. In patients undergoing a liver transplant because of end-stage liver disease due to HBV, there are a variety of posttransplant protocols for prevention of reactivation of HBV (56), many utilizing HBlg. Nonhepatic transplantation in HBsAg positive recipients has been controversial. In the early days of kidney transplantation, such transplants were performed, with some recipients developing early fulminant liver disease and a greater number developing more long-term chronic liver disease (2). Some have maintained asymptomatic status after many years despite evidence of active viral replication (2,57). Then, for a period of time, HBsAg-positive status was considered a contraindication to nonhepatic transplantation. Now, with more effective therapies such as lamivudine available, it appears theoretically possible to transplant such recipients more safely (58) although lamivudine resistance may become an issue (CIII). Adefovir has been successfully used to treat lamivudine-resistant HBV.

Donor and recipient screening: viral infections – Hepatitis C

Hepatitis C virus (HCV) infection is frequently chronic. HCV is a major indication for liver transplantation, and although HCV recurrence is common post-transplant, patient and graft survival are not significantly worse than with other pretransplant diagnoses (59). HCV seropositive renal transplant candidates are at higher risk for liver disease and sepsis after nonhepatic transplants than are their HCV seronegative counterparts (2,57,60), but compared with no transplantation as the alternative, the balance of benefit often falls on the side of transplantation (60). The role of pretransplant viral load reduction is under study. Strategies for management of HCV in the recipient are discussed in detail in a later section.

Hepatitis C positive donors have traditionally been considered a dilemma, because of the high risk of transmission of HCV through transplantation of any organ (61). A positive HCV-RNA, indicative of active viral replication, has been associated with a higher risk of transmission (62), but often this information is not available in the deceased donor time frame. In the future, rapid molecular testing will likely become available in the time frame needed for donor evaluation (61).

The recent Crystal City Meeting emphasized the validity of utilizing the HCV positive donor in certain circumstances, as no increase in 1-year or 5-year mortality or morbidity has been demonstrated in transplanting a liver or kidney from an HCV-positive donor vs. an HCV-negative donor into an HCV-positive recipient (BII) (10,63,64). In recent years, the use of HCV-positive organs for life-saving transplants in HCV-negative recipients has also been studied, sometimes with acceptable results (10,64). A survey of lung transplant programs showed that 55% of programs utilize HCV seropositive donors, in many cases restricted to HCV seropositive recipients (65). A survey of heart transplant programs revealed that only 26% of centers do not use HCV seropositive donors, whereas most other centers utilize these donors for status 1 candidates or HCV-positive recipients, and 64% of centers list HCV positive candidates for heart transplantation (66). However, a recent series identified an excess of rapidly progressive cholestatic hepatitis and an increased mortality for HCV seronegative recipients of donor seropositive heart grafts on mycophenolate-based immunosuppression (67). Whether specific immunosuppressive regimens are preferred in such situations requires further study. In any event, whenever an HCV seropositive donor is utilized, stringent informed consent is advisable.

Donor and recipient screening: viral infections – HIV

HIV-seropositive donors have traditionally not been utilized. HIV-1 and HIV-2 serologies are usually obtained on all potential donors and recipients; HIV-2 is rare in the USA and positive HIV-2 screening serologies are often false-positives. Western blot testing should be obtained for confirmation of any positive screening test for either HIV-1 or 2. Where doubt exists as to a possible exposure for a potential living donor who is HIV seronegative, a molecular viral test should be obtained, which will be positive prior to the development of a positive antibody test. The use of rapidly available molecular testing for HIV is also
desirable for deceased donors when this technology becomes available.

Although previously considered a contraindication to transplantation, HIV seropositivity in the recipient is receiving renewed attention (68–70). Now that many patients with HIV on highly active antiretroviral therapy (HAART) regimens are living longer and with far less immunocompromise, in some cases it is end-stage organ failure rather than HIV which is the survival-limiting condition. A multicenter trial is currently evaluating the feasibility of transplantation in such individuals, with preliminary results being that these transplants are well tolerated with meticulous clinical care and careful attention to pharmacokinetics. The complex issues involved are more fully discussed in the HIV section of these guidelines.

**Donor and recipient screening: viral infections – HTLV-I/II**

Human T-lymphotropic virus 1 (HTLV-I) is endemic in certain parts of the world including the Caribbean and Japan, and is often asymptomatic. However, infection with HTLV-I can progress after years or decades to HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP) or to adult T cell leukemia/lymphoma (ATL); progression occurs in <1% and 2–4% of seropositive individuals in endemic regions, respectively (71). HTLV-II is a virus which is serologically difficult to distinguish from HTLV-I, although its association with disease processes is less certain. PCR assays can be used to distinguish HTLV-I and II if necessary to do so. HTLV-I seropositive donors are generally not utilized, although use of such donors could be considered for a life-threatening situation, particularly in an older recipient, with stringent informed consent (5) (CIII). Although cases of ATL occurring after transplantation have been reported, none was observed in a series of 16 Japanese HTLV-I seropositive recipients undergoing renal transplantation (72).

**Donor and recipient screening: emerging viral infections – West Nile virus and SARS**

West Nile virus (WNV) is a flavivirus which can cause meningocencephalitis, and which has recently appeared in the USA. In the fall of 2002, the CDC’s investigation of transmission of WNV by transplantation to four organ recipients of a single donor was reported (73), and additional reports of transmission by blood transfusion and liver transplantation have appeared (74). It is unclear as yet what the magnitude of the risk of such transmission is, and the pattern of WNV activity is changing on a yearly basis. Serology and PCR for WNV are available but time-consuming. It is prudent to avoid any donor who has had an unexplained, possibly viral illness and/or unexplained mental status changes. Since July 2002, all US blood bank products have been tested for WNV using the investigational nucleic acid amplification test (NAT) which is performed at specific centers. In the fall of 2003, the US Health Resources and Service Administration (HRSA) issued a guidance statement regarding donors and WNV, which recommended testing all prospective live donors with the NAT test close to the time of transplant; avoiding donors with any form of encephalitis; and heightened clinical suspicion on the part of the treating clinician with any febrile illness occurring shortly after transplant. Because of the time currently required to transport samples to centers performing the NAT test, testing of deceased donors is not yet universally recommended, but may be voluntarily undertaken by organ procurement organizations in conjunction with laboratories performing the NAT test. In parts of Canada, testing of donors for WNV IgM as well as the NAT test is being performed.

Since early 2003, the occurrence and spread of SARS (severe acute respiratory syndrome) has been a growing concern. This new respiratory illness appears to be due to a previously undescribed coronavirus, and 10% or more of affected individuals may require mechanical ventilation. The full spectrum of clinical manifestations is still being determined. There is a risk of transmission to health care workers as well as household contacts of affected individuals, and there has been at least one death of a transplant recipient due to SARS. Updated information on SARS epidemiology, infection control, and related topics can be found on the CDC website at http://www.cdc.gov/ncidod/sars and Health Canada’s website at http://www.hc-sc.ca/english/sars. While transmission by transplantation is theoretically possible, the extent of this risk is unknown. Current principles of donor and recipient selection would likely exclude patients with recent acute illnesses meeting SARS criteria; however, the consequences of a more remote history of SARS, or a subclinical illness, are unknown. Screening tools for potential adult and pediatric donors have been proposed and are evolving (University of Toronto Transplant Programs, D. Kumar, A. Humar, and U. Allen, personal communications) which take into account the risk of SARS transmission at the donor’s hospital as well as donor symptoms, travel, and contact history. It is likely that these guidelines will become more formalized as further information is available.

Other new and emerging, potentially communicable agents may arise in addition to WNV and SARS, which may affect donor acceptability or recipient activation on the transplant list. It would be advisable to avoid transplantation involving individuals with potentially communicable infections for which inadequate information exists to provide appropriate recommendations regarding precautionary measures.
Recipient screening: pre-transplant detection of active infection in the recipient

Transplant recipients are at risk for infections related to complications of organ failure (4,7). Patients awaiting renal transplants may have infected hemodialysis or peritoneal dialysis access sites or catheters, or complicated upper- and/or lower-tract urinary infections (8,75,76). Candidates awaiting liver transplants are at risk for aspiration pneumonia, spontaneous bacterial peritonitis, urinary tract infection, and infections associated with intravenous catheters. Candidates awaiting heart transplants may have infections related either to indwelling intravenous catheters, or to ventricular assist devices (VADs) utilized as a bridge to transplantation (see below) (77–83). In addition, heart candidates are also at risk for pneumonia in the setting of congestive heart failure and debilitation.

VAD (ventricular assist-device)-associated infections should be treated prior to transplantation. These infections are common because the VAD is a large foreign body that may be in place for 3 months or longer (77–83). The portal of entry is most frequently the abdominal wall exit site of the drive line. There may be exit site drainage and local infection, more proximal infection in the VAD pocket, bacteremia, and endocarditis. Causative organisms include coagulase-negative staphylococci, Staphylococcus aureus, aerobic Gram-negative bacilli, and yeast. Protracted antibacterial therapy may lead to Candida superinfection. These infections are not a contraindication to transplantation, however, as total removal of the VAD at the time of transplant, combined with appropriate posttransplant antibiotic therapy, is often curative (80,81).

Screening of lung transplant recipients includes an assessment of colonizing airway flora, and careful review of their previous pulmonary infections. Cystic fibrosis patients may be colonized with multiresistant strains of Pseudomonas and/or Burkholderia cepacia (84). There is controversy as to whether patients colonized with Burkholderia should be excluded from receiving lung transplants; molecular typing of Burkholderia isolates is a promising method that may be used to define risk in the future (85,86).

Recipient screening: fungal infections

Pre-transplant colonization with fungal isolates such as Aspergillus is common in lung transplant recipients, particularly in cystic fibrosis patients. Such colonization should prompt a rigorous evaluation to exclude active infection. Although post-transplant aspergillosis is a feared complication, transplant clinicians have generally relied more on posttransplant preemptive and prophylactic strategies (87) rather than pretransplant antifungal therapy for colonized patients. A pretransplant candidate with invasive fungal infection (rather than colonization) should be treated at least until there is radiographic, clinical, and microbiologic resolution in order to minimize the risk of this high-mortality infection posttransplant (AIII).

Pretransplant screening for endemic mycoses is most useful in areas endemic for coccidioidomycosis, where a pretransplant history of active disease and/or seropositivity may prompt lifelong azole prophylaxis (32) (AII). Pretransplant screening for histoplasmosis is of limited value since latent histoplasmosis may be present with a negative serology (DIII); instead, heightened awareness of the possibility of histoplasmosis reactivation is important in when investigating a postransplant febrile illness in a patient from an endemic area.

Recipient screening: mycobacterial infections

All patients should have a PPD (tuberculin skin test) performed prior to transplant, and those who have a positive skin test, or a history of active tuberculosis, should undergo careful additional screening to rule out active disease (see below) (AII). An anergy panel is helpful in interpretation of a negative PPD in patients with end-stage organ disease. Isoniazid hepatotoxicity appears to be less of a problem than originally thought in transplant recipients (28,29), and therefore patients with a history of positive PPD or radiographic evidence of prior TB with no prophylaxis should be considered for isoniazid prophylaxis (28) (AII). Prophylaxis can be started while the patient is on the transplant waiting list; and completed while the patient is on the list or after transplantation. Indeed, it is desirable if at least some of the prophylaxis course can be administered prior to the onset of transplant immunosuppression.

In patients with clinical histories, radiographs, and/or cultures suggesting infection with TB or nontuberculous mycobacteria, the patient should undergo a thorough evaluation for possible active disease, which may include CT scans, bronchoscopy, or other tests as deemed clinically necessary. Any mycobacterial infection should be fully treated with documented microbiologic and radiographic resolution before transplantation is considered.

Recipient screening: parasitic infections

Patients from endemic areas or who have traveled for extended periods of time to endemic areas for strongyloidiasis (including most tropical countries and parts of the south-eastern USA) are at risk for development of disseminated strongyloidiasis after transplant. Although some centers screen with stool ova and parasite examinations, some experts favor screening with serology for Strongyloides which is far more sensitive than stool exams (BIII). For seropositive patients, a short course of thiabendazole or ivermectin is indicated pretransplant, although randomized data are lacking (BIII). As discussed above,
Toxoplasma serology is important in heart recipients, and seronegative heart recipients with seropositive donors should receive prophylaxis (AII). Chagas’ disease and other parasitic infections are more fully discussed in the Parasite Infections section of these guidelines.

Recipient screening: viral infections

Active primary infection with viruses such as CMV, EBV, or HBV at the time of transplant is uncommon. Nonetheless, if active viral infection is detected in a potential recipient (e.g. CMV), it would be wise to delay the transplant until the infection resolves in order to allow for development of natural immunity prior to transplant immunosuppression (AIII). This recommendation also extends to candidates who present for transplantation with clinical symptoms suggestive of an acute community-acquired viral infection. If there is any chance of exposure to HIV pretransplant, the potential recipient should have an HIV molecular detection test as well as HIV antibody testing, because HIV antibody may take 3 months or more to develop (AII). Viral screening of both donor and recipient is discussed in more detail above.

Pretransplant immunizations

The pretransplant evaluation presents an important opportunity to update the potential recipient’s immunizations (4), since many vaccinations are more effective when administered prior to the onset of transplant immunosuppression (88–90) (AII). More detailed immunization recommendations are summarized in a later section of these guidelines.

The varicella-seronegative candidate should ideally be immunized against varicella prior to transplantation (45) (AII). However, if transplantation is expected imminently, it may be best to withhold it as varicella vaccine is a live attenuated vaccine (BIII).

Yearly influenza vaccine should be administered to transplant candidates. (AII). Vaccination of household contacts and health care workers is also very important, as immunocompromised patients may not mount an optimal antibody response to the vaccine (88) (AII). The use of the recently licensed live influenza vaccine should be avoided if transplantation is expected within a month of vaccination.

A hepatitis B vaccine series should ideally be administered pretransplant to seronegative individuals (AII); especially as a potential donor may be found who is HBsAg-negative but HbcAb-positive. Some clinicians have advocated an accelerated course rather than the traditional 3 doses at 0, 1, and 6 months, but further data are awaited. (CIII). The response to vaccine is likely better early on in disease rather than after end-stage organ disease has occurred. Enhanced potency formulations (4) for dialysis patients and others are available (BII).

Patients with advanced liver disease are at particularly high risk for fulminant hepatitis A and should receive hepatitis A vaccination (91) (AII). This vaccine is likely more effective when administered early on in liver disease (92) (BII). The combined hepatitis A and B vaccine is immunogenic but data are awaited in transplant candidates and recipients.

Measles-mumps-rubella vaccine (MMR) is a live vaccine. Patients born in or before 1956 are considered immune due to natural immunity. Patients born after 1956 who have not received a second dose of the MMR vaccine are recommended to receive a second dose, especially if they are in high-risk groups such as health care workers. If administered, MMR should be given pre-rather than posttransplant (BII).

The 23-valent pneumococcal polysaccharide vaccine ideally should also be administered to transplant candidates over the age of 2 who have not received it within the past 5 years (All) (please see Immunizations section for pediatric recommendations). The tetanus-diphtheria toxoid (Td) booster should be administered if the potential adult recipient has not had a Td booster within 5–10 years (AII).

Pretransplant counseling

Prevention strategies for infection should not be limited to medications and vaccinations. A thorough education of the patient and their family members is a very important preventive tool. Pre-transplant classes and printed materials are helpful and should include information on handwashing and other safety measures, environmental exposures, activities to avoid, food safety and handling, foodborne pathogens, pets, and travel (see ‘Strategies for Safe Living Following Solid Organ Transplantation’). It is also helpful for patients to have a general idea of the infections to which transplant patients are susceptible and the prevention strategies in use at their particular center.

Conclusion

Pretransplant screening of the donor and recipient affords an opportunity to assess the safety of the candidate organ, to determine the prophylaxis and preventive strategies utilized posttransplant, to detect and fully treat active infection in the potential recipient prior to transplant, to update the vaccination status of the potential recipient, and to educate the patient and family about preventive measures. Advances in the future will likely include more rapid molecular diagnostic testing to refine the assessment of the risks of transmission posed by a particular donor.
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