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Transplant Infectious Disease: Implications for Critical Care Nurses

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KEYWORDS

- Transplant • Transplant candidates • Transplant recipients
- Organ donors • Ventricular assist devices • Infection
- Infectious disease • Critical care nursing

Solid organ transplantation increases both the length and quality of life for many patients with end-stage organ disease. However, transplantation is not without risk of serious complications, and infection is a major concern in this population. Critical care nurses are frequently involved in the clinical management of potential organ donors, transplant candidates with end-stage organ disease, and transplant recipients. The purpose of this article is to discuss infection in each of these patient populations, particularly with respect to the role of the critical care nurse in preventing, monitoring for, and treating infections.

BACKGROUND

There are several reasons why transplant-related infectious diseases are important to the critical care community. First, there are increasing numbers of immunocompromised patients in the intensive care unit (ICU) because of the improved survival rates of recipients of all types of solid organ transplants (SOTs). As the longevity of transplant recipients increases, these patients are more prone to develop chronic conditions that frequently require ICU stays. Second, the development of novel and more potent immunosuppressive agents has the potential to increase the frequency and severity of posttransplant infections that subsequently necessitate admission to a critical care unit. Lastly, infections in transplant candidates and recipients are a major cause of morbidity, mortality, increased length of hospital stay, and increased costs.¹

INFECTIONS IN TRANSPLANT CANDIDATES

Transplant candidates are often at increased risk of developing infections due to their end-stage disease processes. These patients frequently require ICU care

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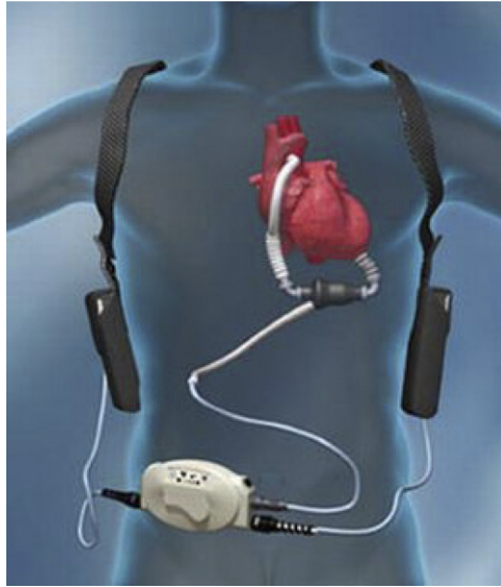


Fig. 1. HeartMate II VAD. (Reprinted from Thoratec Corporation; with permission.)

while they are on the transplant waiting list. Urinary tract infections are common in kidney and pancreas transplant candidates. Kidney transplant candidates are also at risk for infections in the native kidneys and occult abscesses. Liver transplant candidates may have intra-abdominal infections or aspiration pneumonia. Pneumonia is also common in the heart and lung candidate populations. Hospitalized candidates are at risk for catheter- or device-related infections, such as those associated with dialysis access devices or ventricular assist devices (VADs).

Patients With VADs

As of August 2011, there were more than 3100 candidates on the heart transplant waiting list in the United States.² To date, only 949 heart transplant procedures have been performed in the United States in 2011. Thus the demand for donor hearts far exceeds the supply.³ VADs were developed to augment circulation in patients with end-stage heart disease. These devices have been approved by the Food and Drug Administration for three purposes: to bridge patients to heart transplantation, to bridge patients to recovery of their native myocardial function, and to provide permanent support for patients who are not deemed to be suitable heart transplant candidates (“life-time” or “destination” therapy).⁴

VADs can support the right or left ventricle or both. They stabilize the patient’s condition by increasing cardiac output, improving perfusion to vital organs, and restoring mobility.^{5,6} These devices are typically implanted through a median sternotomy incision and placed in a pre-peritoneal or intra-abdominal pocket.

The major components of a VAD are inflow and outflow cannulae, unidirectional valves, a polyurethane chamber (for pulsatile devices), and a pump or rotor. The device is connected to an external power source through a driveline that exits through the abdominal wall (**Fig. 1**).^{7,8}

VADs contain biomaterials and, unfortunately, none of these materials are biologically inert.⁹ Therefore, events that occur at the host-implant interface can trigger aberrant immune activation. When the patient's blood comes in contact with the foreign VAD surface, T cells can become activated and initiate a defective proliferative response and subsequent activation-induced cell death. As a result, the patient's immune system is impaired and the patient may be more susceptible to infection.^{4,5,7,9}

Infection is a common complication of VAD therapy.⁶ VAD-related infections may delay or prevent transplantation altogether and they are a major cause of morbidity and mortality in lifetime therapy patients.¹⁰⁻¹² The most recent International Society for Heart and Lung/Mechanical Circulatory Support Device Registry data indicate that infection occurred in 32.5% of the 655 VAD patients enrolled in this database and that patients with VAD infections had a 7.9% mortality rate.¹³ Device-related infection rates reported in the literature have ranged between 13% and 80%.⁵

Potential infection sites include the surgical site or any component of the VAD (driveline, device pocket, or pump membrane). Driveline infections are the most common; however, more than half of all infections involve several device sites simultaneously.⁷ VAD infections may remain localized or become systemic. If the infection spreads to multiple sites, serious complications such as bloodstream infections, bacteremia, sepsis, and endocarditis can ensue.⁷

Device-, patient-, and mechanical-related factors can contribute to VAD infections. Device-related factors include the exposure of percutaneous drivelines to pathogens and the VAD cavities and pockets that can harbor pathogens. These microorganisms can cause blood flow through the pump to become turbulent; this in turn enables the pathogens to adhere to the surface of the device.⁴ Patient-related risk factors for infection include older age, poor nutritional status, indwelling catheters, prolonged intubation, postoperative bleeding, blood transfusions, multiorgan dysfunction, comorbidities such as diabetes mellitus and obesity, prolonged hospitalization before VAD implantation, and surgical reexploration.^{4,6,7} Mechanical trauma to the driveline exit site is frequently associated with late-onset (>30 days after implantation) infections. Driveline trauma occurs when, for example, the controller or battery pack is dropped or when the driveline is snared on an object. These accidents result in shearing or torsion injuries that can lead to infection.¹²

Device-related infections can occur at any time; however, the majority develop between 2 weeks and 2 months of implantation.⁷ Gram-positive pathogens, particularly *Staphylococcus* species, cause most infections.¹⁴ These organisms are able to form a protective biofilm that blunts the host immune response and enables them to attach to and grow on inanimate surfaces.⁸ Fungal and gram-negative bacilli, such as *Pseudomonas aeruginosa* and the *Enterobacter* and *Klebsiella* species, are other causative agents; these particular pathogens are associated with poorer outcomes.^{4,7} The administration of broad-spectrum antibiotics often leads to the development of fungal infections.⁷

The clinical manifestations of VAD-related infections are varied. Presentation may be subtle or acute. If a device-related infection is suspected, the patient must have a thorough evaluation that includes a comprehensive physical examination and extensive work-up including blood cultures with Gram stains. If possible, cultures should be obtained before initiation of antimicrobial therapy.⁷ Other sources of infection, such as pneumonia, urinary tract or catheter-related infections, must be investigated appropriately. Additional diagnostic tests are site specific. For example, ultrasound is used to evaluate suspected pump pocket infections; transesophageal echocardiograms are useful in the setting of VAD-

related endocarditis. **Table 1** lists the typical signs and symptoms of device-related infections and potential treatment options.

The evidence regarding the impact of device-related infection and posttransplant outcomes is mixed. Some studies have indicated that these infections do not reduce 1-year¹⁵ or overall^{7,16} survival. Other studies have found that serious device-related infections can persist into the posttransplant period^{7,17} and are associated with decreased early¹¹ and long-term¹⁷ posttransplant survival. Although assist devices are often associated with infection, the benefits of this life-saving therapy are thought to outweigh the infection risk.⁷ The major clinical implications for pre- and postoperative nursing care are listed in **Table 2**.

INFECTIONS IN POTENTIAL ORGAN DONORS

Infections can be transmitted via the allograft itself.¹⁸ A donor-derived disease transmission is defined as “any disease present in the organ donor that is or has the potential to be transmitted to at least one of the recipients.”^{19(p234)} Donor-derived infectious diseases are rare. Unexpected transmissions, that is, those that were either unrecognized in the donor or for which the donor was not screened, occur in fewer than 1% of all solid organ transplantation procedures.¹⁹ Although rare, these infections cause significant morbidity and mortality.

Factors that promote infection in potential organ donors include the use of medical devices and the treatment of patients in certain units that have high rates of bacterial contamination.²⁰ It is important to note that treatment of donor infections itself can further increase the potential donor’s risk of iatrogenic infection, for example, via the insertion of intravascular catheters for antimicrobial therapy, the administration of immunomodulating medications such as corticosteroids, and prolonged hospitalization.²¹

Diagnosis of Infection In the Organ Donor

For a number of reasons, infections in potential organ donors may be difficult to diagnose:

- The donor may not have the clinical manifestations of infection due to insufficient numbers or virulence of pathogens.
- Hemorrhage or aggressive fluid resuscitation may dilute both organisms and serologic infection markers such that they are undetectable by conventional laboratory tests.
- The donor may not mount a fever response because brain death causes loss of temperature control and poikilothermia (a phenomenon whereby body temperature decreases to that of the environment).
- The donor’s white blood cell count may be already elevated due to trauma, tissue inflammation, or medications such as corticosteroids.²¹

As a consequence, the diagnosis of infection may rely on culture and urinalysis reports, polymerase chain reaction (PCR) and nucleic acid testing results, characteristics of sputum, and changes in chest radiographs and computed tomography (CT) scans.²¹

Donor Screening

Potential organ donors undergo a rigorous infectious disease evaluation. Organ Procurement and Transplantation Network (OPTN) policies mandate that potential donors must be screened for the following pathogens: human immunodeficiency

Infection Site	Potential Clinical Manifestations	Potential Treatment Options
Driveline	Poor wound healing Fever Leucocytosis Exit site abnormalities: <ul style="list-style-type: none"> • New or persistent serous drainage • Bleeding • Pain • Erythema • Necrosis Induration Nonintegration of driveline Wound dehiscence Simultaneous bloodstream infection	Wound care: <ul style="list-style-type: none"> • Débridement • Bactericidal agent Débridement and vacuum-assisted therapy Targeted systemic antimicrobial therapy Empiric therapy: gram-positive (especially staphylococcal) coverage
Pump pocket	New, persistent drainage from driveline exit site Manifestations of systemic illness: <ul style="list-style-type: none"> • Bloodstream infection • Fever • Leucocytosis Signs of local infection may or may not be present.	Targeted systemic antibiotics Empiric therapy: gram-negative coverage Débridement Open drainage Irrigation Relocation of driveline to clean exit site Implantation of antibiotic beads Replacement of device
Pump endocarditis (infection of any of the pump's surfaces)	Persistent fever Positive blood cultures Clinical manifestations of embolization to other organs (eg, brain, kidney) Progressive cachexia Mechanical problems: <ul style="list-style-type: none"> • Inlet obstruction • Outflow rupture • Bleeding or hematoma within device itself 	Prolonged systemic antimicrobial therapy (4–6 weeks) Replacement of device

Table 2	
Major clinical implications for preventing and treating VAD-related infections^{4,6,14}	
Preoperative	Postoperative
Removal of all unnecessary indwelling lines and catheters	Good handwashing techniques
Close monitoring and reporting of clinical manifestations of infection	Immobilization of the driveline at skin level (eg, with binder) per device manufacturer's recommendations
Maintenance of optimal blood glucose control	Strict sterile technique with cap and mask for dressing changes
Maintenance of adequate nutrition	Meticulous aseptic technique for driveline exit site care following device manufacturer's recommendations
Timely rotation of peripheral lines per protocol	Early extubation and ambulation
Maintenance of good oral hygiene	Removal of all invasive lines, drains, and catheters as soon as possible
Prompt administration of preoperative antibiotics	Prompt discontinuation of prophylactic antibiotics (typically 48 hours after VAD implantation)
Preoperative antiseptic prep per protocol	Close monitoring and reporting of risk factors for (eg, decreased albumin level; hyperglycemia, mechanical stress on wound/driveline) and clinical manifestations of infection
Preoperative clipping (not shaving) of surgical site	For patient with temperature above 38.3 degrees C: obtain and monitor white blood cell count and cultures (blood, sputum, urine)
Nasal culture; for <i>Staphylococcus aureus</i> , administer antibiotic ointment per protocol	Prompt administration of antimicrobial therapy as ordered Maintenance of adequate nutrition Maintenance of optimal blood glucose control Timely rotation of peripheral lines per protocol Maintenance of good oral hygiene

virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis, human T-lymphotropic virus (HTLV), cytomegalovirus (CMV), and Epstein-Barr virus (EBV). Blood and urine cultures are required for donors who have been hospitalized longer than 72 hours.²² Potential heart donors are screened for toxoplasmosis. Many donors are also screened for nosocomial infections such as methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci. Because infection can be transmitted via transfusions, serologic testing is typically performed both before and after a potential donor receives blood products. In addition, family members are questioned about the potential donor's infection risk, including prior infection exposure, history, and immunizations; travel to endemic areas; and risky behaviors such as intravenous drug abuse. **Table 3** displays donor organ acceptance and exclusion criteria based on the results of infectious disease screening.

Table 3**Acceptance or exclusion of donor organs based on infectious disease testing²³**

Evidence of	Action
Active tuberculosis	Exclude from donation
Active systemic fungal infections	
Active rabies	
Active lymphocytic choriomeningitis	
West Nile virus or other encephalitis	
Antibody to human immunodeficiency virus	
Antibody to HTLV I/II	Generally exclude from donation except in life-threatening situations and with the recipient's informed consent
Hepatitis B surface antigen (Hepatitis B surface antigen positive or Hepatitis B core antibody IgM positive)	Generally exclude from donation except in life-threatening situations, with recipient prophylaxis and with the recipient's informed consent
Antibody to hepatitis C virus	Use only for recipient with antibody to HCV or for a severely ill recipient and with recipient's informed consent
Antibody to cytomegalovirus (CMV): base prophylaxis on recipient's CMV serostatus	Generally safe
Antibody to Epstein-Barr virus (EBV): Monitor EBV polymerase chain reaction if recipient is EBV seronegative	
Hepatitis B surface antibody (HBsAb) positive	
Rapid plasma reagin positive: Recipient should receive prophylaxis with penicillin	
<i>Toxoplasma</i> antibody positive: Seronegative heart transplant recipients should receive prophylaxis with trimethoprim/sulfamethoxazole (Bactrim; Septra); if recipient is allergic to sulfa, pyrimethamine (Daraprim) is used	

The acceptance of organs from donors with known infections with or exposure to HIV, hepatitis, or other viruses remains controversial.²¹ Given that the number of transplant candidates on the waiting list far exceeds the number of available organs, strategies to expand the donor pool include accepting donors with certain infections, higher-risk serological profiles, and social histories suggestive of prior exposure to bloodborne infections as well as donors who may be more at risk for transmitting infections (eg, older donors and donors with long ICU stays).²⁰ Informed consent

Box 1**Principles of antibiotic selection and administration for potential organ donors²¹**

1. Select a bactericidal antibiotic over a bacteriostatic antibiotic.
2. Use medication that will most directly target the identified bacteria to prevent the removal of harmless bacteria, the promotion of selective overgrowth of fungi, resistant organisms, or abnormal bacterial strains (eg, *Clostridium difficile*), and the development of gene mutations and highly resistant organisms.
3. Substitute directed antibiotic for broad-spectrum agent once sensitivities are available.
4. Follow Organ Procurement Organization antibiotic protocols for antibiotic selection.
5. Initiate empiric antibiotics when the potential risk of infection is high (eg, for open wounds, facial/sinus fractures, pyuria) or in the setting of suspected bacterial infection (eg, suspicious chest radiograph findings; purulent sputum).
6. Base antibiotic selection on intensive care unit-specific tabulation of species and sensitivities (antibiograms).
7. Consider use of two antibiotics with different mechanisms of action to achieve additive synergy against gram-negative and gram-positive bacteria.
8. Consider empiric antibiotics for methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococci (VRE) in the ICU setting.
9. Consider antibiotics specifically effective against anaerobic bacteria in the setting of facial injuries, pulmonary aspiration, or contaminated wounds from an injury scene.
10. Administer antibiotics intravenously to maximize bioavailability.
11. Adjust antibiotic doses in the setting of renal failure, hepatic failure, and older donor age.

mandates that potential recipients be informed of the donor's infection status and the risk of infection transmission associated with that particular donor.²³

Treatment of Infection In Potential Organ Donors

Effective treatment of bacterial infections in potential organ donors can result in successful transplantation.²¹ **Box 1** displays important principles of antibiotic selection and administration for potential organ donors.

Role of the Organ Procurement Coordinator

The organ procurement organization's (OPO's) coordinator has major responsibilities regarding the prevention and treatment of infections and reporting known infections to transplant centers that could potentially receive organs from infected donors. Infections that must be reported to the transplant center are listed in **Box 2**. Moreover, all antimicrobial agents that are given to the potential donor must be documented and reported to each transplant center that receives an organ from that donor.²¹

Donor-Derived Disease Transmission

When a transplant center is informed that one of its organ recipients is confirmed positive for or has died from a potential donor-derived transmissible disease, that center must notify, within one working day, the OPO that procured that organ. The OPO must then notify the OPTN. These reports are forwarded to UNOS and uploaded to the Disease Transmission Advisory Committee's (DTAC's) secure website.

Box 2**Infections that must be reported to the transplant center³⁵**

Known conditions that may be transmitted by the donor organ must be communicated to the transplant center. These may include, but are not limited to, the following:

- Unknown infection of central nervous system (encephalitis, meningitis)
- Suspected encephalitis
- Hepatitis C
- Herpes simplex encephalitis or other encephalitis
- History of JC virus infection (causes progressive multifocal leukoencephalopathy)
- West Nile virus infection
- Cryptococcal infection of any site
- Rabies
- Creutzfeldt–Jacob disease
- Other fungal or viral encephalitis
- Bacterial meningitis
- Infection with human immunodeficiency virus (HIV) (serologic or molecular)
- Active viremia: herpes, acute EBV (mononucleosis)
- Serologic (with molecular confirmation) evidence of human T-lymphotropic virus (HTLV-I/II)
- Active hepatitis A or B
- Infection by *Trypanosoma cruzi*, *Leishmania*, *Strongyloides*, *Toxoplasma*
- Active tuberculosis
- Severe acute respiratory syndrome (SARS)
- Pneumonia
- Bacterial or fungal sepsis (eg, candidemia)
- Syphilis
- Multisystem organ failure due to overwhelming sepsis, such as gangrenous bowel
- Any new condition identified by the Centers for Disease Control and Prevention (CDC) as being a potentially communicable disease
- Any aspects of the donor's medical or social history that might increase the risk of disease transmission
- Donors at high risk for transmission of HIV

DTAC data indicate that, between 2005 and 2007, there were 80 donors with reported possible donor-derived infectious disease transmission, 30 recipients with confirmed (proven, probable, or possible) donor-derived infections, and 14 recipient deaths attributed to donor-derived infections. These deaths were due to hepatitis C, tuberculosis, HIV, Chagas disease, bacteremias, candidemia, *Strongyloides*, and lymphocytic choriomeningitis virus.¹⁸

INFECTIONS IN TRANSPLANT RECIPIENTS

There are three major factors that determine a transplant recipient's risk of infection. These include the patient's epidemiological exposure, either in the

hospital or in the community; the patient's current antimicrobial regimen, if any; and the patient's net state of immunosuppression, which is defined as "the combined effect of all of the factors that determine the patient's susceptibility to infection."^{24(p138), 25} The net state of immunosuppression includes the patient's current immunosuppressive regimen (number and strength of antirejection agents), as well as any of the following concurrent factors: infection with an immunomodulating virus (eg, CMV or EBV); metabolic or autoimmune disorders (eg, diabetes mellitus); neutropenia or lymphopenia; disruption of mucocutaneous barriers; and surgical sequelae (eg, fluid collections).²⁵

Types of Infections

Approximately 80% of all transplant recipients have at least one significant infection during the first posttransplant year.²⁶ The three major groups of posttransplant pathogens are bacteria, viruses, and fungi (**Fig. 2**). Bacterial infections are the most common,²⁶ followed by viral and fungal infections.

Bacterial infections

Bacterial infections frequently occur at the transplant site. Bacterial pneumonias are common among all types of solid organ transplant recipients. Nosocomial pathogens of particular concern include *Clostridium difficile*, vancomycin-resistant enterococcus, methicillin-resistant *Staphylococcus aureus*, and extended-spectrum β -lactamase gram-negative bacilli. Common organ-specific bacterial infections and associated risk factors are listed in **Table 4**.

Viral infections

Most posttransplant viral infections are caused by two groups of pathogens: the herpes viruses (CMV, EBV, HSV 1 and 2, and varicella zoster) and the hepatitis viruses. Viral infections are particularly deleterious because they have both direct and indirect effects. The direct effect is the clinical syndrome caused by the virus itself, such as CMV pneumonia or hepatitis. Indirect effects include potential injury to the allograft, rejection, oncogenesis, and the virus's ability to alter the net state of immunosuppression, thereby increasing the patient's susceptibility to other opportunistic infections. The herpes viruses are characterized by latency. This means that once the virus is present, the patient will harbor the viral genome for life. Immunosuppression, particularly augmented immunotherapy in the setting of rejection, can trigger replication of latent herpes viruses.²⁴

Cytomegalovirus is the most important pathogen that affects transplant recipients. There is a bidirectional relationship between CMV and rejection. CMV can trigger rejection and the inflammatory effects of rejection and rejection therapy can increase CMV viral replication. The allograft is more likely to be affected by a CMV infection than a native organ. Thus, liver transplant recipients with CMV infections are prone to develop vanishing bile duct syndrome, heart transplant recipients are at risk for coronary artery vasculopathy, lung transplant recipients are at risk for bronchiolitis obliterans, and so forth. The most common types of CMV disease are hepatitis, pneumonitis, and gastroenteritis. With regard to CMV serostatus, the risk of developing a posttransplant CMV infection is highest in CMV-seronegative recipients who receive an allograft from a CMV-seropositive donor and lowest in CMV-seronegative recipients who receive an allograft from a CMV-seronegative donor. Recipients who receive potent antirejection therapy such as antithymocyte globulin are also at increased risk for developing a CMV infection. A concurrent critical illness can lead to the reactivation of a latent CMV infection; this is thought to be associated with

MEDICAL PROGRESS

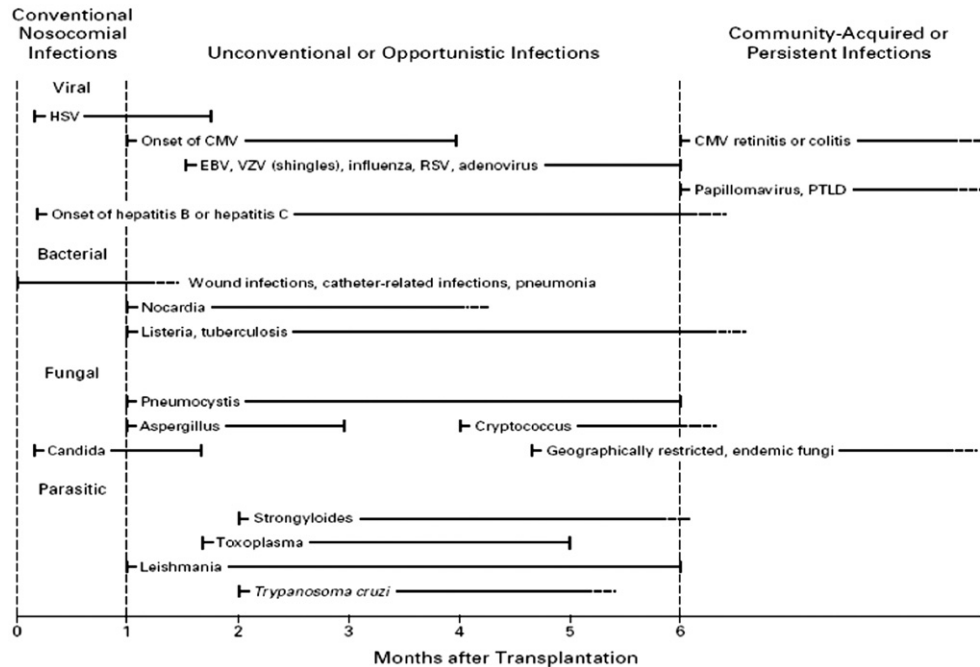


Fig. 2. Usual timeline of infections after organ transplantation. Exceptions to the usual sequence of infections after transplantation suggest the presence of unusual epidemiologic exposure or excessive immunosuppression. *Abbreviations:* CMV, cytomegalovirus; HSV, herpes simplex virus; PTLN, posttransplant lymphoproliferative disease; RSV, respiratory syncytial virus; VZV, varicella zoster virus. Zero indicates the time of transplantation. Solid lines indicate the most common period for the onset of infection. Dotted lines and arrows indicate periods of continued risk at reduced levels. (Adapted from Fishman A, Rubin RH. Medical progress: infection in organ transplant recipients. *N Engl J Med* 1998;338 (24): 1741-1751. Copyright© 1998. Massachusetts Medical Society; with permission.

Table 4
Organ-specific bacterial infections and risk factors

Type of Transplant	Common Types of Bacterial Infections	Risk Factors
Lung, Heart–lung ^{29,36}	Pneumonia Mediastinitis Sternal wound infection Anastomotic infections—may be secondary to placement of bronchial stents	Impaired cough reflex Poor mucociliary clearance Abnormal lymph drainage Disruption of phrenic nerve Prolonged mechanical ventilation Ischemia Reperfusion injury Bacterial colonization secondary to rejection-mediated airway inflammation Single-lung transplantation: infection in native lung
Liver ^{37,38}	Intra-abdominal (liver, biliary tract, peritoneal cavity) Surgical wound Cholangitis Abscesses Device-related Urinary tract Respiratory Bacteremia	Prolonged operative time; reoperation Blood transfusions Early rejection CMV infection Retransplantation Roux-en-Y choledocojejunostomy (due to reflux of intestinal material and microbial flora into the biliary system)
Kidney ^{24,29}	Urinary tract Surgical wound Infected lymphocele	Diabetes mellitus Renal insufficiency Prolonged urinary catheterization Neurogenic bladder Decreased urine flow Anatomic abnormalities Risk factors for recurrent urinary tract infections: <ul style="list-style-type: none"> • Serum creatinine >3 mg/dL • Prednisone dose >20 mg/day • Multiple treated rejection episodes • Chronic viral infections

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Table 4 (continued)		
Type of Transplant	Common Types of Bacterial Infections	Risk Factors
Heart ²⁴	Pneumonia Mediastinitis Sternal wound	Prolonged mechanical ventilation Prolonged intensive care unit stay Disruption of phrenic nerve Decreased pulmonary protective mechanisms Surgical reexploration Retransplantation
Pancreas, Kidney-pancreas ^{39,40}	Wound infection Intra-abdominal abscess Urinary tract infection Cystitis Peritonitis	Diabetes mellitus Kidney/pancreas transplant: anatomic reanastomosis of allograft Anatomic placement of organ: rate of deep wound infections higher with retroperitoneal placement than with intraperitoneal placement Prolonged urinary catheterization Neurogenic bladder Acidic pancreatic enzymes can cause anastomotic erosion and peritonitis Risk of cystitis higher with bladder drained pancreas due to effect of pancreatic enzymes
Intestine ³⁰	Device-related Pneumonia Translocation of bacteria from allograft to: <ul style="list-style-type: none"> • Peritoneal cavity • Portal circulation • Splanchnic venous system Bacterial overgrowth	Preoperative liver disease and/or sepsis Leakage associated with division of the lymphatics during procurement Preservation injury to intestinal epithelium Prolonged ischemic time; reperfusion injury Prolonged operative time; reoperation Inability to close abdominal wall Rejection High levels of immunosuppression Transplantation of intestinal contents and gastrointestinal flora with allograft Multiple invasive lines and catheters

proinflammatory cytokines and subsequent downregulation of the immune system. Agents used to prevent or treat CMV infection include ganciclovir, valganciclovir, acyclovir, and CMV immune globulin. Foscarnet is often used to treat ganciclovir-resistant organisms. Because CMV can be transmitted through blood transfusions, CMV-seronegative transplant candidates and recipients should receive CMV-negative, leukocyte-poor, or filtered blood products.^{1,24}

Given that most adults are EBV-seropositive, most posttransplant EBV infections in adults are reactivated from latent pretransplant infections. However, EBV-seronegative recipients can acquire an EBV infection through blood transfusions or community exposure. The incidence of posttransplant EBV infections is highest in multiorgan and intestinal transplant recipients followed, in decreasing order, by kidney–pancreas, lung, heart, liver, and kidney recipients. Intravenous ganciclovir has been used as preemptive therapy for patients at high risk for EBV infections, for example, patients receiving antilymphocyte antibody therapy for rejection. The clinical sequelae of EBV infection range from a relatively mild mononucleosis-like syndrome to posttransplant lymphoproliferative disease (PTLD). Treatment options for mononucleosis include acyclovir. PTLD is a set of syndromes that ranges from a benign, self-limiting polyclonal proliferation of B cells to an aggressive, malignant, monoclonal lymphoma. Risk factors for PTLD include pretransplant EBV-negative serostatus, primary EBV infection, high EBV viral load, CMV serostatus mismatch (recipient is CMV negative and donor is CMV positive), CMV disease, potent rejection treatment, and type of allograft. The incidence of PTLD is highest in intestinal transplant recipients. Treatment options for PTLD range from antiviral agents (acyclovir, ganciclovir) and decreased immunosuppression for the benign polyclonal form to chemotherapy, radiation, resection, and decreased immunosuppression for malignant monoclonal lymphoma.

Fungal infections

Although invasive fungal infections have the lowest incidence of all infections, they are associated with the highest morbidity and mortality rates.²⁷ Risk factors for fungal infections include the use of high-dose corticosteroids and broad-spectrum antibiotics, rejection that requires increased immunosuppression, allograft dysfunction, and a simultaneous infection with an immunomodulating virus such as CMV.²⁴

Two genera, *Aspergillus* and *Candida*, cause the vast majority of posttransplant fungal infections. Together, these two pathogens account for more than 80% of invasive fungal infections. These infections typically present during the first month posttransplant,²⁷ but they can occur at any time. The most common fungal infection that involves the respiratory tract is invasive aspergillosis, which may affect approximately 30% of solid organ transplant recipients.²⁸ Other portals of entry include the gastrointestinal tract and the skin. The risk of disseminated candidiasis is highest in neutropenic patients with central venous catheters who have received broad-spectrum antibiotics and who have had prolonged ICU stays.²⁹ Liver transplant recipients are at highest risk for invasive candidiasis, followed, in decreasing order, by pancreas, lung, heart–lung, kidney, and heart transplant recipients.²⁹

INFECTIONS IN PEDIATRIC TRANSPLANT RECIPIENTS

Pediatric transplant recipients are often at higher risk for posttransplant infections for a number of reasons, including:

- Lack of immunity to common pathogens such as CMV and EBV
- Incomplete immunizations

- Increased technical difficulty and prolonged transplant operative time due to pretransplant palliative surgeries
- Inability to close the abdomen or chest due to placement of a large allograft into a small child
- Social behavior of children in densely populated day care and school settings.³⁰

MEDIASTINITIS

Acute mediastinitis can develop after the implantation of mechanical circulatory assist devices or after heart, lung, and heart–lung transplantation. The risk of posttransplant mediastinitis is higher if the patient had a mechanical circulatory assist device or a total artificial heart as a bridge to transplantation. There are preoperative, intraoperative, and postoperative risk factors for mediastinitis. Examples of preoperative risk factors include diabetes mellitus, prior sternotomy, renal failure requiring dialysis, prolonged hospitalization before the transplant surgery, and obesity. The risk of developing mediastinitis is more than double in patients with a body mass index greater than 30. Intraoperative risk factors include blood transfusions and prolonged cardiopulmonary bypass, aortic cross-clamp, and operative times. Examples of postoperative risk factors include surgical reexploration, prolonged ICU stay, prolonged mechanical ventilation (>24–48 hours), having a tracheostomy, cardiopulmonary resuscitation, poor perioperative and postoperative glucose control, and low posttransplant cardiac output.³¹

The major etiologic pathogens associated with mediastinitis include, in decreasing order, gram-positive cocci (*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus* spp., *Streptococcus* spp.), gram-negative bacilli (*Escherichia coli*, *Enterobacter* spp., *Klebsiella* spp., *Proteus* spp., other Enterobacteriaceae, and *Pseudomonas* spp.), and fungi (*Candida albicans*).³¹

The initial clinical manifestations of mediastinitis may be subtle: mild chest pain, and edema or erythema along the sternal incision.²⁴ The most common presenting symptom is fever; it may be associated with localized infection, erythema, cellulitis, purulent drainage, pleuritic-like pain, and sternal instability. Diagnostic studies include CT scans, cultures, and laboratory tests. Laboratory findings include elevations in the white blood cell count, C reactive protein, and procalcitonin. The latter test is particularly useful in distinguishing between rejection and infection. Once mediastinitis is diagnosed, treatment should be initiated promptly. Therapeutic options include surgical drainage/débridement, wound irrigation, tailored parenteral antimicrobial agents, and nutritional support.³¹

NEUROLOGIC INFECTIONS

In transplant recipients, central nervous system (CNS) infections are among the most deleterious because they can be difficult to diagnose and treat. Diagnosis is often challenging because presenting symptoms, such as mental status changes, seizures, focal neurologic deficits, and headache, may be blunted by immunosuppressive therapy. Moreover, the neurotoxic effects of antibiotics, antiviral agents, and immunosuppressants themselves may make diagnosis even more complicated.^{32,33}

The first step in diagnosing a suspected CNS infection is a neuroimaging study to establish the presence, location, potential etiology, and characteristics of any lesion(s). Magnetic resonance imaging studies of the brain or spinal cord or both are typically preferred to CT scans. Neuroimaging studies are useful in determining if the infection is focal or nonfocal and if it involves the meninges. Other diagnostic tests include cerebrospinal fluid analyses, electroencephalograms, viral polymerase chain

reaction tests, cultures, and serologic tests. Brain biopsies are rarely done, except in the setting of posttransplant lymphoproliferative disease and brain abscesses. The posttransplant interval, patient-specific risk factors, and the timing and evolution of clinical manifestations also help to inform the diagnosis.³²

CNS infections may be caused by fungi, viruses, or bacteria. Fungal infections carry the highest mortality rate—90% or higher—of all pathogens.³² Most brain abscesses are associated with *Aspergillus*. These abscesses tend to occur early in the posttransplant period, particularly in recipients who have multiple risk factors for infection such as surgical reexploration, dependence on mechanical ventilation or dialysis, or retransplantation.³³ Unlike meningitis in immunocompetent patients, posttransplant meningitis is typically caused by fungi. In this setting, the patient often develops a systemic infection that subsequently spreads to the CNS. Viral CNS infections may be associated with the reactivation of a latent virus, such as JC virus-induced progressive multifocal leukoencephalopathy, or they may be caused by a new exposure to a pathogen such as West Nile virus. Other pathogens commonly associated with posttransplant encephalitis include the herpes simplex virus, varicella zoster virus, EBV, and CMV. Bacterial CNS infections are more frequently caused by *Listeria* and *Nocardia* rather than more common bacterial pathogens.³²

Due to the severity of CNS infections in transplant recipients, an infectious disease consult, coupled with prompt diagnosis and treatment, is imperative. Empiric, broad-spectrum antimicrobial agents are typically administered until the causative organism is identified.³²

FEVER

Immunosuppressive agents blunt the inflammatory response to infection; however, in most cases, transplant recipients with infections will have an increase in temperature. Some infections, however, tend to occur in the absence of fever. These include *Pneumocystis* pneumonia, focal fungal lung infections, and cryptococcal meningitis.²⁹

Patients with a persistent fever greater than 38°C or acute pulmonary infiltrates or both are typically hospitalized for an infection workup. Fevers of unknown origin are most commonly associated with CMV or EBV viral syndromes. It is important to note that fevers in transplant recipients may also be caused by drug reactions (particularly antilymphocyte therapy), pulmonary emboli, deep vein thrombosis, and rejection. Rejection-induced fever typically occurs in lung transplant recipients. It occurs less commonly in kidney and liver transplant recipients and rarely in heart recipients.^{24,29}

CARE OF TRANSPLANT DONORS, CANDIDATES, AND RECIPIENTS: IMPLICATIONS FOR CRITICAL CARE NURSES

Given that other human beings are the most frequent source of infection in the patient's environment, it is essential that nurses prevent the nosocomial transmission of respiratory viruses and the transmission of organisms through contaminated hands or inanimate objects.²⁹ In addition, it is important for critical care nurses to:

- Follow standard precautions
- Use aseptic techniques with vascular and urinary catheters
- Ensure that ventilator circuits, catheters, and dressings are changed per protocol
- Inspect all percutaneous catheter sites for signs of infection
- Maintain closed systems for urinary and suction catheters
- Keep the head of the bed elevated to decrease the risk of aspiration.

- Restrict access to patients by visitors and staff with colds or other contagious illnesses
- Avoid transporting transplant recipients through areas of hospital construction
- Promptly recognize and report the clinical manifestations of infections
- Obtain and report diagnostic test results in a timely manner
- Administer and document antimicrobial agents in a timely manner
- Assess and report the vaccination status of transplant candidates and recipients
- Know the CMV, EBV, and other pertinent serostatuses of the donor and recipient.^{21,29}

SUMMARY

Infection is an important issue for critical care nurses as they care for patients throughout all phases of the transplant continuum: potential organ donors, transplant candidates, and transplant recipients. This article has reviewed salient issues relative to infections in each of these patient populations, including patients with VADs, and has highlighted key points pertaining to bacterial, viral, and fungal infections.

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