



Management and prophylaxis of bacterial and mycobacterial infections among lung transplant recipients

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Abstract: Bacterial and mycobacterial infections are associated with morbidity and mortality in lung transplant recipients. Infectious complications are categorized by timing post-transplant: <1, 1–6, and >6 months. The first month post-transplant is associated with the highest risk of infection. During this period, infections are most commonly healthcare-associated, and include infections related to surgical complications. The lungs and bloodstream are common sites of infections. Common healthcare-associated organisms include methicillin-resistant *Staphylococcus aureus* (MRSA), Gram-negative bacilli such as *Pseudomonas aeruginosa*, and *Clostridioides difficile*. More than 1-month post-transplant, opportunistic infections can occur. Tuberculosis occurs in 0.8–10% of lung transplant recipients which reflects variation in background prevalence. The majority of post-transplant tuberculosis stems from reactivation of untreated or undiagnosed latent tuberculosis. Most post-transplant tuberculosis occurs in the lungs and develops within a year of transplant. Non-tuberculous mycobacteria commonly colonize the lungs of lung transplant candidates and are often hard to eradicate even with prolonged courses of antimycobacterial agents. Drug interactions between antimycobacterial agents and calcineurin and mTOR inhibitors also complicates treatment post-transplant. Given that infection adversely impacts outcomes after lung transplant, and that anti-infective therapy is often less effective after transplant, infection prevention is key to long-term success. A comprehensive approach that includes pre-transplant evaluation, perioperative prophylaxis, long-term antimicrobial prophylaxis, immunization, and safer living at home and in the community, should be employed to minimize the risk of infection.

Keywords: Bacterial infection; mycobacterial infection; lung transplant; long-term management; prophylaxis

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Introduction

After nearly a half century since the first lung transplant in 1963, the number of lung transplants performed worldwide has increased considerably and now approaches 6,000 transplants annually (1). While it is life-saving for patients with end stage lung disease, 5-year survival after lung transplant is still around 50% which is less than that of other solid organ transplants (2,3). Analysis of an international

registry of 60,107 lung transplants performed between 1990 and 2016 showed that infection was the second most common cause of death after graft failure (2). It accounted for 16.5–36.8% of deaths depending on time from transplant and was highest (36.8%) between 31 days to 1 year (2). Bacterial infections are most common (4). Improvement in management and prevention of bacterial infections is of paramount importance in the care of lung transplant

recipients. In this review, we focus on bacterial and mycobacterial infections and emphasize their management and prevention in the long-term.

Risk, type, and timing of infection

The risk of infection for lung transplant recipients is largely affected by two major factors: net state of immunosuppression and epidemiologic risk factors (5). Factors contributing to the net state of immunosuppression include immunosuppressive therapy, prior therapies including chemotherapy and antimicrobials, mucocutaneous barrier integrity, neutropenia, technical complications, underlying immune defects, metabolic complications, and viral infections. In general, risk of rejection is highest in the early post-transplant period, thereby necessitating intense immunosuppressive therapy immediately post-transplant. Although lung transplant recipients require life-long immunosuppressive therapy, maintenance immunosuppression becomes less intense over time.

Lungs have direct contact with the environment and therefore are continuously exposed to various pathogens. After lung transplant, denervation of the allograft results in decreased mucociliary clearance and cough, leading to decreased local host defense mechanisms. In addition, although there is substantial variation among transplant centers, roughly a third of patients undergo lung transplant for interstitial lung disease, which often requires long-term immunosuppressive therapy even before transplant (2). Another fifth of patients have bronchiectasis as a primary indication, mostly cystic fibrosis (2). Since most patients with cystic fibrosis are colonized or infected with drug resistant Gram-negative bacteria, they often receive multiple courses of antibiotics pre-transplant. Important epidemiological exposures pertinent to bacterial and mycobacterial infections include donor-derived infections, recipient-derived infections, nosocomial infections, and community-acquired infections (6). Donor-derived and recipient-derived infections are now rare because of pre-transplant screening, evaluation, and treatment of bacterial and mycobacterial infection. However, cases of donor-derived pulmonary tuberculosis in lung transplant recipients have been reported (7-10).

The timing of post-solid organ transplant infection is often categorized into three different time periods by time from transplant; <1, 1–6, and >6 months (5,6). The first month post-transplant is associated with the highest risk of infection. During this period, infections are most

commonly healthcare-associated, and include infections related to surgical complications. In addition, donor-derived infections and preexisting recipient infections (recipient-derived infections) can occur. Among bacterial and mycobacterial pathogens, antimicrobial resistant species including methicillin-resistant *Staphylococcus aureus* (MRSA), Gram-negative bacilli such as *Pseudomonas aeruginosa*, and *Clostridioides difficile* are often involved. In patients with preexisting structural lung diseases like cystic fibrosis, glucose non-fermenting Gram-negative bacilli such as *P. aeruginosa* or *Burkholderia cepacia* can be colonizers pre-transplant and often resistant to multiple agents. These organisms can be a culprit of infection early post-transplant. Between the first and sixth months after transplant, patients are at the highest risk of opportunistic infections. Prophylaxis with trimethoprim-sulfamethoxazole is used widely and has reduced the incidence *Pneumocystis* infection. Trimethoprim-sulfamethoxazole also has activity against *Nocardia* and *Listeria monocytogenes*. Nocardiosis and listeriosis can occur during and after this period especially without prophylaxis with trimethoprim-sulfamethoxazole. Similarly, infections from mycobacterial infections (both tuberculous and non-tuberculous infections) can occur during and after this period. After six months post-transplant, pneumonia from community-acquired pathogens, most commonly *Streptococcus pneumoniae*, become more important as immunosuppressive regimens are tapered and stable in most cases.

Although this schema of post-transplant infections is useful, variation exists in real-world clinical care. For instance, if a patient has protracted surgical complications, healthcare-acquired infections can occur after one month. If a patient has allograft rejection requiring augmentation of immunosuppression, the patient remains at high risk of opportunistic infections after six months post-transplant.

Common sites of infections

Pneumonia

Pneumonia remains the most frequent complication for lung transplant recipients, with about a third of recipients developing pneumonia post-transplant (11-14). Pneumonia is associated with significant mortality (13). Its incidence is highest in the first month and decreases gradually over time (13,15). Pneumonia is predominantly from bacterial pathogens, especially Gram negative bacilli such as *P. aeruginosa*, *Acinetobacter baumannii*, and *Enterobacteriaceae*

(12,13,15-17). Differential diagnoses for post-transplant pneumonia is broad and includes infectious (bacterial, mycobacterial, fungal, viral, and parasitic) and non-infectious etiologies. A systematic approach to stratify risk and orient therapy is needed (18). Initial evaluation involves obtaining key clinical history such as recent hospitalizations and exposures, as well as laboratory and radiologic studies. Depending on the risk for opportunistic infections and severity of illness, additional studies such as sputum culture for bacterial and mycobacterial pathogens, interferon gamma releasing assay, *Legionella* antigen and tissue specimen testing may be performed to guide empiric and targeted therapy.

Bacteremia

The bloodstream is the second most common site of bacterial infection (12,14). The lungs and vascular catheters are common sources (19). In addition to Gram-negative bacilli, Gram-positive cocci such as *S. aureus*, coagulase negative *Staphylococcus*, and *Enterococcus* can also cause bacteremia (20).

Bacterial infections

Staphylococcus aureus

S. aureus is an important pathogen in lung transplant recipients, and affects about a fifth of patients (21,22). Of those, about 40% are methicillin-resistant (22). The respiratory system and bloodstream are the most common sites of infection (21-23). *S. aureus* infections are associated with increased mortality and graft rejection (22). Risk factors include isolation of MRSA from recipient's sterility cultures, and MRSA cultures from the nares or respiratory tract at the time of transplant (22). In light of the high prevalence of MRSA infections among lung transplant recipients, vancomycin is often used for perioperative prophylaxis (24). A computer simulation model study suggested that screening and decolonization of MRSA among lung transplant recipients would be cost-effective (25). However, further research is needed before active surveillance can be recommended (24). In the meantime: (I) adherence to hand hygiene among patients, families, and healthcare workers; (II) universal decolonization with chlorhexidine bathing for patients in intensive care units; (III) disinfection of patient equipment and the hospital environment are recommended to reduce MRSA transmission and infections (24).

Pseudomonas aeruginosa

P. aeruginosa is an important pathogen for lung transplant recipients because of its prevalence and tendency to develop drug resistance. It is a common colonizer seen in over 30% of lung transplant recipients and is the most common cause of post-transplant pneumonia accounting for a quarter of cases (13,26). Pre-transplant colonization with *P. aeruginosa* is also common among patients with structural lung diseases, especially cystic fibrosis (27). Up to 45% of them are multidrug resistant strains (28). Post-transplant airway colonization with *P. aeruginosa* is associated with subsequent development of bronchiolitis obliterans syndrome, which is a major cause of death among lung transplant recipients (26,27). Although post-transplant infections with multidrug resistant *P. aeruginosa* poses a significant challenge, survival rates are comparable regardless of its presence (29) and pre-transplant colonization with multidrug resistant *P. aeruginosa* is not an absolute contraindication to transplant (30). If a transplant recipient has a history of *P. aeruginosa* colonization, at least two antipseudomonal agents based on previous antibiotic susceptibility results should be continued for 2 to 3 weeks post-transplant (31). Colistin and aminoglycosides are agents often used for prophylaxis and treatment of multidrug-resistant *P. aeruginosa*. However, they have cumulative nephrotoxicity especially with concomitant calcineurin inhibitor use. Newer agents such as ceftolozane-tazobactam or ceftazidime-avibactam might be options but their role in lung transplant recipients is yet to be defined (32,33). Use of inhaled colistin and aminoglycosides as adjunctive therapy to intravenous agents for prophylaxis and treatment of post-transplant infection with multidrug resistant *P. aeruginosa* in lung transplant recipients has been reported in case series (34-36). However, more studies are needed to evaluate its efficacy and safety.

Clostridioides difficile

The incidence of *C. difficile* infection (CDI) in lung transplant recipients is 1.9–22.9% (37-43) and is highest of all solid organ transplant recipients (44,45). Besides the early post-transplant period, CDI has a second peak after 24 months (42). CDI has been associated with increased mortality among lung transplant recipients (37,42). The diagnosis and treatment of CDI are generally the same as non-transplant recipients (45). Details regarding management are available in guidelines (45). Reducing unnecessary antibiotic use through antimicrobial

stewardship programs, decreasing use of gastric suppressing agents, avoiding prolonged hospitalization, and increasing adherence to contact precautions when necessary are recommended strategies for CDI prevention (45). The role and safety of probiotics have not been established in lung transplant recipients (46).

Nocardia

Nocardiosis is an important infection in lung transplant recipients. *Nocardia* species are found in soil, freshwater, saltwater, and decaying vegetation worldwide. There are more than 40 species that cause human infection that have unique geographic distributions and antimicrobial susceptibility patterns. The incidence of nocardiosis is 1.9–3.5% in lung transplant recipients which is highest of all solid organ recipients (47–49). In a retrospective study of 473 lung transplant recipients, nocardiosis occurred a median of 34 months post-transplant (50). Its incidence has decreased due to trimethoprim-sulfamethoxazole use intended as *Pneumocystis* prophylaxis (51); however, there are reports of breakthrough nocardiosis from isolates susceptible to trimethoprim-sulfamethoxazole (50). Subacute nodular or cavitary lung lesions are its most common manifestations. In addition, nocardiosis has a propensity to involve the central nervous system, typically in the form of single or multiple brain abscesses. Patients may or may not have neurological symptoms; therefore, radiographic evaluation of the brain is necessary if a patient has nocardiosis outside of the central nervous system. Skin and soft tissue infections, as well as disseminated infections have been described (49). The diagnosis of nocardiosis requires isolation of *Nocardia* from specimens obtained from suspected sites of infection. Because antimicrobial susceptibility is highly variable among species and isolates, isolation with accurate speciation of *Nocardia* is crucial. It is recommended that incubation be prolonged with selective media; that molecular methods are used for speciation; and that clinicians communicate with the clinical microbiology laboratory (52). The antimicrobial regimen depends on the susceptibility pattern of the causative isolate, as well as site and severity of infection. Trimethoprim-sulfamethoxazole is the agent of choice if the isolate is susceptible. Mild to moderate infections can be treated with trimethoprim-sulfamethoxazole alone; in contrast, at least two agents (typically imipenem-cilastatin or amikacin in addition to trimethoprim-sulfamethoxazole) are required for severe infection, central nervous involvement or disseminated

diseases (52). The recommended duration of therapy is 6–12 months or longer dependent on the site and extent of infection as well as the degree of immunosuppression (52). Trimethoprim-sulfamethoxazole may be useful for preventing primary and relapsed nocardiosis; however, the optimal dose and duration are not well defined (52).

Mycobacterial infections

Tuberculosis

The reported incidence of tuberculosis in lung transplant recipients is 0.8–10% (53–59), likely reflecting variation in background prevalence. In a Spanish multicenter study of 4,388 solid organ transplant recipients, lung transplant recipients were 5.6 and 73.3 times higher risk than other solid organ transplant recipients and the general population respectively (60). Most post-transplant active tuberculosis is reactivation of untreated or undiagnosed latent tuberculosis (61). Less than 5% are donor-derived and very few constitute primary infection (61). Most post-transplant tuberculosis occurs in the lungs and develops within a year (56,59,60). In cases of donor-derived tuberculosis, pulmonary tuberculosis develops within 3–6 months post-transplant (62). Diagnosis of active tuberculosis in lung transplant recipients is similar to non-transplant patients. Given that its clinical manifestations and radiographic findings are non-specific, a high index of suspicion coupled with additional invasive procedures to obtain specimens when necessary are needed. The treatment for active tuberculosis among lung transplant recipients is the same as non-transplant patients. Daily dosing is strongly recommended (61).

Screening and treatment of transplant candidates and donors are important. However, more than a half of transplant candidates who later develop tuberculosis might show anergic or negative responses to tuberculin skin testing (56). For lung transplant candidates with positive tuberculin skin tests or interferon gamma release assays, therapy for latent tuberculosis should be provided after active tuberculosis is ruled out. Lung transplant candidates who are at high epidemiologic risk, such as close contacts of persons with active tuberculosis and/or radiographic evidence of prior tuberculosis without adequate treatment, should be considered for latent tuberculosis therapy. Isoniazid for 9 months is the recommended regimen for latent tuberculosis in solid organ transplant candidates (61). One study involving 398 lung transplant candidates

reported comparable safety and efficacy with a 3-month regimen with isoniazid and rifampin (63).

Non tuberculous mycobacteria (NTM)

NTM infection is a unique challenge to lung transplant candidates and recipients for several reasons. First, structural lung disease, which can be the indication for lung transplant, is a risk factor for NTM infection (64). Second, NTM is often hard to eradicate even with prolonged courses of antimycobacterial agents. Furthermore, drug interactions between antimycobacterial agents and calcineurin and mTOR inhibitors are problematic post-transplant. Finally, pre-transplant colonization with NTM, especially *Mycobacterium abscessus* or *Mycobacterium avium complex* (MAC), is associated with NTM disease and increased mortality post-transplant (65).

The reported incidence of NTM infection is 0.46–8.0% in lung transplant recipients, and primarily involves the lungs (55,57,66–68). Among NTM, MAC and *M. abscessus* are the most common (69). The isolation of NTM, most commonly MAC, *M. abscessus*, and *M. goodii* post-transplant is much more common than actual infection and can be seen in up to 22.4% of lung transplant recipients (66). Lung transplant itself is the strongest risk factor for post-transplant NTM infections (70,71). Other risk factors include African-American race and cytomegalovirus mismatch status (67). Up to 80% of NTM infections in lung transplant recipients involve the lungs and pleural spaces, followed by cutaneous/soft tissue and disseminated infections (72). In a cohort study of 34 solid organ transplant recipients (19 of 34 were lung transplant recipients) with post-transplant NTM infections, the median diagnosis from transplant was 8 months (71). Diagnosis of NTM infection requires fulfillment of clinical, radiographic, and microbiological criteria similar to non-transplant recipients (73). However, diagnosis is often not straightforward. NTM airway colonization is common, making it difficult to differentiate disease from colonization. Furthermore, common lung colonizers of immunocompetent patients, such as *M. goodii*, can be a pathogen in lung transplant recipients. Indeed, isolation of the same species on multiple occasions is associated with treatment among lung transplant recipients (70).

Antimicrobial therapy for NTM infections in lung transplant recipients is extrapolated from that in non-transplant patients (73,74). The regimen differs by species and generally consists of two to three or more drugs.

Details of antimicrobial therapy for NTM infections are beyond the scope of this review and readers are invited to review published guidelines (73,75). Of note, rifabutin and azithromycin are preferred over other rifamycins and macrolides because of less drug-drug interactions with calcineurin/mTOR inhibitors through CYP3A4 (74). Treatment duration depends on extent of disease and clinical response, and is often prolonged. For pulmonary NTM infections, therapy is continued for at least 12 months after respiratory cultures become negative (74). Decreasing immunosuppression when feasible and surgery for localized disease are important adjunctive treatment (74).

To reduce the risk of post-transplant NTM infection and ensure antimicrobial regimen tolerability, it is recommended that lung transplant candidates be treated pre-transplant to eradicate NTM infection if possible, or at least reduce mycobacterial burden (74). In addition, bilateral lung transplant, and/or minimizing spillage of native lung contents into the pleural cavity are recommended (74). After lung transplant, rinsing fiberoptic endoscopes with tap water should be avoided (74). Lung transplant recipients should be advised to avoid hot tubs or exposure to soil, dust, and plant material after hospital discharge (74).

Prevention

Given that infection adversely impacts outcomes after lung transplant, and that anti-infective therapy is often less effective after transplant, infection prevention is vital to the care of lung transplant patients. Attention should be paid to multiple preventive strategies at time periods described below.

Pre-transplant evaluation

Pre-transplant evaluation to assess risk of infection for candidates and donors can prevent transmission of donor-derived pathogens, reactivation of preexisting pathogens, and surgical site infections. Standard evaluation consists of obtaining (I) thorough history that includes underlying lung disease, prior treatment, prior infections and their treatment, comorbidities, places of travel/residence, occupation, and exposure to animal and environmental pathogens; (II) physical examinations; (III) standard blood, microbiological, and radiographic studies (76). Depending on the history, further studies may be warranted. As part of standard screening, tests for syphilis [fluorescent *Treponema* antibody absorption (FTA-ABS), *T. pallidum* particle agglutination (TPPA), *T. pallidum* enzyme immunoassay

(TP-EIA), rapid plasma reagin (RPR), Venereal Disease Research Laboratory (VDRL)], and tuberculosis (either purified protein derivative or interferon gamma releasing assay) are recommended for transplant candidates and living donors (76). If either or both are reactive, a transplant candidate or donor needs to be assessed for latent or active infection and treated accordingly pre-transplant. Respiratory cultures pre-transplant can guide perioperative antimicrobial prophylaxis, especially for patients with cystic fibrosis who are well known to be colonized with multidrug resistant organisms. In particular, patients colonized with *Burkholderia cepacia* genomovar III (*cenocepacia*) are at increased risk for poor outcomes after lung transplant (57). Colonization or infection with *Burkholderia cepacia* complex and *M. abscessus* are relative contraindications for lung transplant (77,78). For deceased donors, respiratory cultures with bronchoscopy, as well as blood and urine cultures are also recommended (76).

Perioperative prophylaxis

Surgical site infections occur in 5–19% of lung transplant recipients (79–82), and can present as soft tissue infection, mediastinitis, and airway anastomosis infection (83). In addition, early post-transplant pneumonia is even more common (79,84). Data to guide optimal perioperative prophylaxis to prevent surgical site infection in lung transplant recipients are scarce. Clinical practice guidelines for antimicrobial prophylaxis in surgery developed by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America recommend first generation cephalosporins as agents of choice (85). However, Gram negative bacilli such as *Pseudomonas*, *Burkholderia*, and *Enterobacteriaceae* as well as *Staphylococcus* and *Enterococcus* are common causative organisms for surgical site infection. Because of this, vancomycin plus a third generation cephalosporin or cefepime are often used (83). Patients allergic to penicillin can be given levofloxacin instead. Given that recipients or donors can be infected or colonized with drug resistant organisms pre-transplant, perioperative prophylaxis should be tailored according to their microbiology and risk factors for surgical site infection. Antibiotics must be administered within 60 minutes (120 minutes for vancomycin or levofloxacin) before the incision (85,86). The optimal duration is yet to be defined but the guidelines from the American Society of

Transplantation recommend 48–72 hours (83).

Long term prophylaxis

Trimethoprim-sulfamethoxazole is recommended primarily for the prevention of *Pneumocystis* pneumonia and continued life-long for lung transplant recipients (87). Since it has activity against *S. pneumoniae*, *Staphylococcus*, *Enterobacteriaceae*, *L. monocytogenes*, and *Nocardia*, trimethoprim-sulfamethoxazole is useful for the prevention of bacterial infections. Breakthrough infections from these organisms have been reported (50). Of note, in cases where an antibiotic other than trimethoprim-sulfamethoxazole is used for the prevention of *Pneumocystis* pneumonia, antibacterial prophylaxis is not recommended. Therefore, clinicians should be aware of higher risk for infections from organisms typically covered by trimethoprim-sulfamethoxazole.

Immunization

All lung transplant candidates should have up to date vaccinations according to national guidelines prior to transplant (88,89). Because lung transplant recipients cannot mount an immune response to vaccination post-transplant due to immunosuppression, efforts should be made prior to transplant. The optimal immunization schedule for lung transplant candidates or recipients has not been studied; however, age, type of organ, and local epidemiology should be taken into account (90). Live-attenuated vaccines are not administered to lung transplant candidates receiving immunosuppressive medications and lung transplant recipients. Inactivated vaccines can be given pre-transplant and post-transplant. Live-attenuated and inactivated vaccines should be given at least 4 and 2 weeks prior to transplant to resolve vaccine-related viral replication and ensure adequate immune response respectively (88). The optimal time to restart immunization post-transplant is not well-defined; yet, immunization is typically restarted 3–6 months post-transplant provided there is no ongoing rejection and immunosuppression has stabilized. Vaccinations should not be withheld out of concern for allograft rejection if there is no ongoing rejection (88).

Regarding pneumococcal vaccination, both the 13-valent protein-conjugate vaccine and the 23-valent polysaccharide vaccine are indicated. If a lung transplant recipient has never received PCV13 or PPSV23, they can be given post-transplant. If a candidate or recipient has never received

either vaccine, a single dose of PCV13 followed 8 weeks later by a PPSV23 is recommended pre-transplant in vaccine-naïve patients (88,89). A PPSV23 booster can be given after 5 years.

Recommendations for vaccination of adult solid organ transplant candidates and recipients against bacterial pathogens from the American Society of Transplantation are summarized in *Table 1* (89). If a lung transplant recipient plans for international travel, careful assessment and planning including risk-based immunization prior to travel is warranted (91).

Living donors should also be up to date with vaccinations according to national guidelines although vaccination for donors solely for the recipients' benefit is not recommended (88). Healthcare workers and close contacts of transplant recipients should also be vaccinated (88). In general, inactivated vaccines are preferred but live-

attenuated vaccines can be given (except for oral polio and smallpox) as long as enhanced infection prevention precautions such as handwashing are performed.

Safe living

Most lung transplant recipients are at home and living with stable immunosuppressive regimens. While infections cannot always be avoided, practical advice can be given to patients when at home, work, or school. Infections 6 months post-transplant are often community-acquired; avoiding exposures is imperative. Key areas for prevention include infections transmitted by direct contact, droplet/aerosol, ingestion, animal contact, sexual contact, and occupational exposure. Recommendations for safer living by solid organ transplant recipients from the American Society of Transplantation are summarized in *Table 2* (92).

Table 1 Recommendations for vaccination of adult solid organ transplant candidates and recipients against bacterial pathogens from the American Society of Transplantation (89)

	Live-attenuated or Inactivated	Before transplant	After transplant
Tetanus	Inactivated	Recommended	Recommended
Pertussis (Tdap)	Inactivated	Recommended	Recommended
<i>Haemophilus influenzae</i> type B	Inactivated	Recommended	Recommended
<i>Streptococcus pneumoniae</i> (conjugate vaccine)	Inactivated	Recommended	Recommended
<i>Streptococcus pneumoniae</i> (polysaccharide vaccine)	Inactivated	Recommended	Recommended
BCG	Live attenuated	Recommended	Not recommended
Anthrax	Inactivated	Not recommended	Not recommended

Table 2 Recommendations for safe living by solid organ transplant recipients with regards to prevention of bacterial and mycobacterial infections from the American Society of Transplantation (92)

Type of infection	Common causative organisms	Strategies
Infections transmitted by direct contact	<i>Clostridioides difficile</i>	Frequent and thorough handwashing especially when touching mucous membranes
	Non tuberculous mycobacterium	Wear gloves whenever handling heavily contaminated materials
		Avoid going barefoot outside
		Wear shoes, socks, long pants, and long-sleeved shirts while doing gardening, yard work, farming, or being in parks or wooded areas
		Avoid self-piercing or tattooing or sharing of needles

Table 2 (continued)

Table 2 (continued)

Type of infection	Common causative organisms	Strategies
Respiratory infections	<i>Mycobacterium tuberculosis</i>	Avoid close contact with persons with respiratory illnesses
	<i>Pseudomonas aeruginosa</i>	Avoid crowded areas
		Avoid tobacco or marijuana smoke
		Avoid activities and occupational settings that increase the risk of exposure to tuberculosis
		Wear a mask if exposure to above high-risk areas is unavoidable
Food safety	<i>Escherichia coli</i> 0157:H7	Avoid the following:
	<i>Salmonella</i>	<ul style="list-style-type: none"> ● Drinking unpasteurized milk, fruit, or vegetable juice/cider
	<i>Brucella</i>	<ul style="list-style-type: none"> ● Eating cheeses made with unpasteurized milk
	<i>Listeria</i>	<ul style="list-style-type: none"> ● Eating raw or undercooked eggs
	<i>Yersinia</i>	<ul style="list-style-type: none"> ● Ingesting raw seed sprouts ● Cross-contamination when preparing food ● Eating uncooked pate, meat spreads, cold cuts, and smoked seafood ● Eating from public salad bars or buffets, street vendors, picnics ● Eating any food prepared by someone with a recent diarrheal illness
Animal contact related infections	<i>Enterobacteriaceae</i>	Avoid contact with animals that have diarrhea
	<i>Chlamydophila</i>	Take the pet regularly to the veterinarian for checkups
	<i>Pasteurella</i>	Avoid cleaning bird cages, bird feeders, litter boxes, and handling animal feces
	<i>Capnocytophaga</i>	Avoid stray animals
	<i>Mycobacterium marinum</i>	Avoid animal bites and scratches
		Wear gloves to clean aquariums or have someone else in the household do the cleaning
Sexually transmitted infections	<i>Treponema pallidum</i>	Always use latex condoms outside of long term monogamous relationship or during periods of immunosuppression
	<i>Neisseria gonorrhoea</i>	Avoid exposure to feces during sexual activity
	<i>Chlamydia trachomatis</i>	
Work and school related infections		Seek guidance from transplant teams and/or transplant infectious disease consultants regarding the following:
		<ul style="list-style-type: none"> ● The optimal timing of returning to work or school ● Mitigating potential infectious risks in the workplace ● Reported outbreaks of infections in the workplace or at school

Conclusions

Bacterial and mycobacterial infections are important problems associated with morbidity and mortality in lung transplant recipients. Comprehensive approaches starting at the time of transplant evaluation and continued through post-transplant periods are required to minimize the risk of infection and optimize the management of infectious complications.

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Footnote

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