Safe Living Following Solid Organ Transplantation

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KEYWORDS

• Solid organ transplantation • Vaccination • Food safety • Travel advice
• Infection prevention

KEY POINTS

- Infections after transplant can have significant impact on a patient's as well as their organ's survival. Several strategies can be used to minimize risk of acquisition of such infections.
- Vaccination against viral and bacterial illnesses, carefully timed preferably pretransplant, as well as safe living strategies posttransplant can afford protection against infections.
- Careful assessment pretransplant combined with a strategy of ongoing patient education pretransplant and posttransplant can assist patients with maintaining their health.

INTRODUCTION

Living safely after organ transplantation requires an integrated care continuum that starts before transplant and ideally even before the development of end organ disease. In order to minimize a solid organ transplant (SOT) recipient's risk for infection and risk for injury, it is important to anticipate the risks after transplantation inherent in living. These risks include potential exposure to others with viral or bacterial illness, to food and water sources, participation in recreational activities, resuming sexual activity, living with pets, and opportunities for travel, especially internationally. It is invaluable to orient potential SOT recipients to these risks, because often leading up to transplant they may likely experience debilitation and significant handicaps due to chronic illness. After SOT, once they overcome the preceding debilitation and surgical effects, they, despite chronic immunosuppression, can go on to live healthy, fruitful lives, which they may not have been able to fully conceive of while debilitated. Thus, in anticipation of SOT, potential transplant recipients should update their vaccinations. Potential recipients need to be made aware of food and water safety important after transplant so they may plan accordingly. In addition, potential recipients

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should be educated as to the risks of pet ownership and animal exposure, again to plan accordingly. Finally, realistic expectations should be set with regard to travel and participation in recreational activities especially within the first year after transplant, the period during which they are at increased risk of infection.[1] The American Society for Transplantation Infectious Diseases Community of Practice has previously set forth informal guidance on strategies for living safely after SOT.[2] The investigators astutely note that, unlike Centers for Disease Control and Prevention (CDC) guidelines set forth in other populations such as hematologic stem cell transplant recipients[3] and those infected with human immunodeficiency virus,[4] no such evidence-based guidance exists for the SOT population. That said, the data available for these groups and other immunocompromised populations can be extrapolated to provide guidance, understanding that this guidance may require tailoring based on an individual patient's situation.[2]

STRATEGIES TO PREVENT INFECTION

Vaccination

Posttransplant infections can have a major effect on a patient's as well as their allograft's survival; thus strategies aimed at preventing infections are likely to have significant impact.[5] One such strategy is vaccination (please see Dr Christian Donato-Santana and Nicole M. Theodoropoulos' article, "Immunization of Solid Organ Transplant Candidates & Recipients: A 2018 Update," in this issue for more details). Although inactivated vaccinations have been demonstrated safe after SOT, so too are these vaccines safe in end-stage liver disease (ESLD) and end-stage renal disease (ESRD), and antibody titer response after vaccination is higher pretransplant.[6–12] Viral infections, such as measles virus and varicella zoster virus that can be prevented by live-attenuated vaccine, can have significant morbidity and mortality after SOT.[13] Varicella disease in the immunocompromised host can lead to severe complications.[14,15] Measles outbreaks unfortunately continue to occur in the present day, and measles in an immunocompromised host can cause pneumonitis and encephalitis and has been associated with high mortality.[16]

Live-attenuated vaccines are not recommended posttransplant; thus, identifying those susceptible hosts pretransplant and vaccinating them are paramount in avoiding devastating consequences of infection in an SOT recipient. Most transplant centers have procedures in place to identify these susceptible patients via pretransplant serologies, and every effort is made to ensure vaccination occurs before transplant with intervals as prescribed by the Advisory Committee of Immunization Practices (ACIP). Two other vaccine-preventable diseases that are more common than measles require attention: influenza and *Streptococcus pneumoniae*. Because invasive pneumococcal disease can have substantial morbidity and mortality in SOT recipients and in those with chronic lung, heart, renal, and liver disease, the ACIP recommends vaccination with PCV13 followed by PPSV23. Furthermore, there are few contraindications to influenza vaccine in these populations, especially given the severe pulmonary and extrapulmonary complications associated with infection.[5] Live-attenuated influenza vaccine should be avoided posttransplant both in the SOT recipient and, if at all possible, in their household contacts.[17]

In general, in anticipation for SOT, vaccination should occur as soon as possible to afford protection to those with chronic heart, lung, renal, and liver disease but also because live-attenuated vaccinations should not be administered after transplant. Realistically, however, this is not always possible because in those with critical illness, there may not be time to complete vaccination series before transplant. However,

transplantation should not be postponed solely for this purpose. Although the optimal timing of vaccination after transplantation is not known, most centers initiate vaccination 3 to 6 months after transplantation.[17] Despite theoretic concerns, no evidence of a link to vaccination and acute episodes of rejection has been found.[14,18,19] Thus, influenza vaccine should be administered yearly as long as at least 3 to 6 months after SOT and not given previously that season. Ideally, any encounter with a potential SOT recipient should prompt a review of vaccine status and update as indicated[5] (**Table 1**).

Everyday Strategies for Disease Prevention

In SOT, most infections occur during the first 6 months after transplant unless there are extenuating circumstances, such as organ rejection and need for augmentation of immunosuppression. After 6 months, most infections seen in the SOT recipient are similar to those seen in the general adult population.[1] Because most pathogens are either acquired via direct contact via hands, ingestion, or inhalation, frequent hand washing and avoidance of those with respiratory or gastrointestinal illnesses are essential ways to minimize acquisition of infectious pathogens.[2] Close contacts of transplant recipients should be encouraged to receive updated vaccines as per the ACIP guidelines and their personal health care providers. There is little risk from family members/close contacts who receive live-attenuated vaccines to transplant

Table 1
Vaccine recommendations

Vaccine	Schedule	Comments
Influenza	Annually	Pretransplant & posttransplant
Hepatitis B	3 doses	Consider 40-μg dose in ESLD & ESRD
Hepatitis A	2–3 dose series depending on vaccine	Recommended in ESLD & high-risk travel
Tdap	Single dose ≤2 y after last Td	Td booster every 10 y thereafter
Pneumococcal		
Prevnar (PCV13)	Once regardless of age	If given after PSV23, then wait ≥1 y
Pneumovax (PPSV23)	≥8 wk after PCV13	If administered before age 65, then booster after 5 y
Varicella	2 dose series if nonimmune	Pretransplant only
MMR	1–2 doses depending on previous vaccination	Pretransplant only
Shingles (Varicella-Zoster)		
Zostavax	Once in adults >50 y	Pretransplant only; may be obsolete with advent of Shingrix
Shingrix	To be determined	Approved by FDA 10/20/17 & voted on by ACIP 10/27/17; official recommendations in immunocompromised hosts pending
HPV	3 doses through age 26	Catch up if not previously vaccinated as child
Meningococcal (MenACWY)	1–2 doses	Only for certain populations per ACIP guidelines & no immunogenicity studies post transplant

Data from Refs.[5,17,20,21]

recipients. The only exceptions are smallpox and oral polio vaccines, which are very rarely indicated.[17] In addition, even with rotavirus vaccine, SOT recipients could refrain from diaper changing and/or use meticulous hand washing rather than not have their close contact vaccinated.[22] Similarly, review of safe sexual practices with SOT recipients can reduce risk for acquisition of several pathogens, including hepatitis B and C, human immunodeficiency virus, herpes simplex virus, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, syphilis, and other fecally transmitted organisms. Unless the patient is in a long-term monogamous relationship, condom usage should be advised. Furthermore, SOT recipients should be counseled on avoidance of oral exposure to feces and hand hygiene after sexual intercourse.[2,3] **Table 2** lists other approaches and habits to use to avoid contact with environmental objects/individuals to decrease an SOT recipient's chance of exposure to infectious pathogens.

Food and Water Safety

According to the CDC, 48 million persons get sick; 128,000 are hospitalized, and 3000 die from food-borne infection and illness in the United States each year. The most often impacted are those with weakened immune systems,[23] which is why education and guidance should be directed at potential SOT recipients and reiterated frequently after transplantation. Waterborne infections arise from drinking contaminated drinking water or inadvertent ingestion of water during recreational activities, such as boating, enjoying water parks, or swimming.[2] Access to safe drinking water within the United States is as simple as using water from the tap delivered from and US Environmental Protection Agency–regulated public water system.[24] That said, many people in the United States who receive their water from private ground water wells are thus responsible for ensuring their water is free from contaminants.[24] The most common causes of water-associated disease outbreaks due to private water sources per the CDC as of 2010 are as follows[24]:

- Hepatitis A
- Giardia

Table 2
Avoidance strategies against environmental and opportunistic pathogens

Employ hand washing after:	Avoid:
Eating or preparing food	Close contact with persons with respiratory viruses
Changing diapers	Prolonged contact with crowded areas
Touching plants or dirt	Tobacco and marijuana smoking
Using the restroom	Visiting areas with increased risk of exposure to tuberculosis (prisons, homeless shelters, certain health care facilities)
Touching animals, particularly at zoos or fairs	Construction areas/areas of excavation
Touching items in contact with animal or human bodily fluids	Areas with possible exposure to fungal spores: caves, barns, bird cages/coops, soil aerosols via mulching
Collecting or deposing of garbage	Self-piercing, tattooing, or needle sharing
Going outdoors or to a public place	

Data from Avery RK, Michaels MG, the AST Infectious Diseases Community of Practice. Strategies for safe living after solid organ transplantation. Am J Transplant 2013;13:304–10; and Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. Biol Blood Marrow Transplant 2009;15(10):1143–238; and *Adapted from* https://www.fda.gov/downloads/Food/FoodborneIllnessContaminants/UCM312793.pdf.

- Campylobacter
- Shigella
- *Escherichia coli*
- Cryptosporidium
- Salmonella
- *Yersinia enterocolitica*

Thus, private water sources such as these should be avoided by SOT recipients.[2] In addition, SOT recipients should avoid swimming in recreational facilities that are likely to be contaminated with human or animal waste, and if swimming, avoid swallowing such water.[2]

After transplant, many patients may experience a renewed appetite that was suppressed due to previous chronic illness such as ESLD or ESRD. Food safety is paramount to retaining an SOT recipient's health with attention paid to handling, preparing, and consuming foods.[25] Raw fish and meats should be handled on separate surfaces from other food items.[3] Separate cutting boards should be used for each food item or thoroughly washed with soapy warm water between uses for separate foods.[3] Any person preparing raw foods as an SOT recipient or for an SOT recipient should practice meticulous hand hygiene after handling raw foods.[3] Raw vegetables should be washed thoroughly before ingestion. Even fruits with skins should be washed before cutting or peeling to avoid internal contamination from the surface.[25] Canned foods should have the lids washed before opening to avoid contaminating the inner contents.[25] All cooked foods should be heated to US Department of Agriculture–recommended safe minimum internal temperatures, including reheating previously cooked foods, such as hams and deli meats.[25] These practices are simple ways to decrease risk of the many infections outlined in **Table 3**, which can have more fulminant presentations and/or be more difficult to treat and eradicate in SOT recipients. Unfortunately, many of these illnesses present similarly; thus, knowledge of potential risk behaviors can inform the SOT recipient on what to avoid, and if ill, can be highlighted to the care team as a possible source of infection/symptoms.

Pet Safety and Animal Contact

Studies have demonstrated the health benefits of animal-human bonding, especially in the immunocompromised, who may feel isolated as a result of their underlying illnesses.[28] Physicians should advise SOT recipients of the potential risks inherent in pet ownership and animal contact, although in most circumstances, such ownership/contact is not absolutely contraindicated.[3] The SOT recipient should not feed or pet stray animals. In general, pets such as lizards, snakes, turtles, baby chicks/ducklings, and exotic pets should be avoided because of risk of *Salmonella* and *Campylobacter* infections.[28–30] Specific guidance for the care of pets should include the following: feeding pets only high-quality commercial food, not raw meat or raw eggs; allowing pets to drink only from potable water sources; leashing and confining dogs to prevent coprophagy (eating feces); avoiding juvenile cats or dogs because they are more prone to enteric infections.[28] In addition, although routine veterinary care for pets is important, SOT recipients can be at risk for pet vaccines–related illness, and thus, caution must be advised. The "kennel cough" vaccine, which is a mixture of *Bordetella bronchiseptica* and parainfluenza, can pose infection risk.[28,30] The *Brucella* animal vaccine has been associated with human illness.[30] In addition to the risks potentially prevented by obtaining veterinary care, caution must be advised when providing in home pet hygiene. In general, bird cages and litter boxes should be cleaned daily by someone other than the SOT recipient. Although fish are

Table 3
Major pathogens causing food-borne illness in solid organ transplant

Food-Borne Pathogen	Commonly Associated Source	Most Common Symptoms/ Complications in SOT
Campylobacter	Contaminated water; raw meat/ poultry; unpasteurized milk	Diarrhea (often bloody), fever, nausea; can lead to bacteremia
Cryptosporidium	Contaminated (unwashed) food; contaminated drinking/ recreational water	Crampy, watery diarrhea leading to dehydration; in SOT can be prolonged
Listeria monocytogenes	Unpasteurized milk/cheeses; improperly reheated deli meats/ hot dogs; store-bought meat salads	Abdominal pain; diarrhea; fevers; chills; headache; can lead to bacteremia and meningitis
E coli	Undercooked meat; contaminated water; unpasteurized juices	Diarrhea; vomiting; certain strains can lead to hemolytic uremic syndrome
Salmonella	Undercooked meat, poultry, eggs; unpasteurized milk/juices; pet turtles	Abdominal pain; fever; diarrhea (may be bloody); can lead to bacteremia
Toxoplasmosis gondii	Raw & undercooked meats (including deer); handling cat feces	Mononucleosis-like symptoms; severe systemic disease in SOT
Vibrio vulnificus	Undercooked & raw seafood	Diarrhea, nausea, vomiting; severe sepsis in SOT
Norovirus	Contaminated food or water; close contact with infected individual	Watery diarrhea (can be prolonged in SOT), nausea, acute onset vomiting

Data from Refs.[25–27]

generally a lower-risk pet, care must be applied to cleaning of fish tanks because mycobacterial disease associated with skin and soft tissue has been linked to such activities.[28–30] Finally, after any animal contact, whether with a personal pet or at a zoo or aquarium, all individuals, but most importantly SOT recipients, should practice careful hand washing.[28–30]

Travel Advice

As per the CDC, immunocompromised travelers compose 1% to 2% of the travelers seen in US travel clinics.[31] These visit statistics are important to note because travel to destinations outside of North America and Europe are associated with increased exposure to enteric and vector-borne pathogens.[32] In a large travel clinic study in Canada from 2001, two-thirds of the travelers surveyed who were SOT recipients were foreign born[32] and historically, being foreign born increases a traveler's likelihood of staying with friends and family.[32] As such, it is unclear if foreign-born SOT recipients frequent travel clinics as several studies have indicated that those traveling to visit friends and family are more likely to contract travel-related illnesses because they are less aware of their susceptibility, less likely to seek pretravel advice, and adopt higher risk behaviors.[33–35] Because of these data, education and recommendation toward seeking pretravel advice should be targeted at all SOT recipients because improved pretravel consultation can potentially prevent devastating infections.[36] The CDC recommends that several key education points be discussed with

immunocompromised travelers: developing an illness contingency plan with an identified clinic/hospital; bringing extra medications in case of travel delay; avoiding procuring medications during travel due to risk of counterfeit; use of sun protection; vigilant food and water precautions; and travel with a health kit.[31] In addition to these measures, travel to high-risk destinations should be postponed until at least a year after transplantation.[31] If a potential SOT recipient has the potential to travel to yellow fever–endemic areas after transplant, consideration should be given to vaccination before transplantation.[36] In addition, household contacts of SOT recipients can and should receive live-attenuated travel vaccinations before travel with the precautions as described above in the vaccination section.[32] As for the SOT travelers themselves, other inactivated or non–live vaccines for typhoid, hepatitis A, hepatitis B, and meningococcus should be administered as indicated.[36] In addition, malaria chemoprophylaxis should be prescribed for SOT recipient travelers to endemic areas because they are by virtue of the SOT susceptible to more serious disease.[31] Care does however need to be used when prescribing malaria chemoprophylaxis because potential drug-drug interactions with immunosuppressive medications and dose adjustment for altered renal or hepatic function need to be considered.[31] In addition, strict vector precautions should be advised because diseases like Chagas and leishmaniasis can disseminate in immunocompromised hosts.[36] Furthermore, Dengue infection accounts for about 10% of the systemic febrile illnesses experienced by travelers, suggesting that SOT recipients would be similarly affected.[37] In addition, Chikungunya and Zika viruses have emerged as important travel-associated vector-borne infections recently. Thus, information about the severity in immunocompromised travelers is still being ascertained.[36] Although such extensive travel counseling may be perceived as excessive especially by those who are foreign born, such measures may assist with preventing substantial life-altering illness by promoting travel yet in the safest way possible.

SUMMARY

Receipt of an organ transplant will most likely extend the recipient's life substantially, and, it is hoped, this extension is associated with good health. The benefits of longevity by virtue of organ transplantation need to be closely protected by education before, during, and after transplantation about potential risks and measures to mitigate such exposures. The topics addressed here ensure that an SOT recipient and their providers can plan accordingly and implement measures that will assist with maintaining such health.

REFERENCES

1. Snydman DR. Epidemiology of infections after solid-organ transplantation. Clin Infect Dis 2001;33(Suppl 1):S5–8.
2. Avery RK, Michaels MG, the AST ID COP. Strategies for safe living after solid organ transplantation. Amer J Trans 2013;13:304–10.
3. Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. Biol Blood Marrow Transpl 2009; 15(10):1143–238.
4. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents. AidsInfo.NIH.gov. Available at: https://aidsinfo.nih.gov/guidelines on 12/26/2017. Accessed January 1, 2018.
5. Chow J, Golan Y. Vaccination of solid-organ transplantation candidates. CID 2009;49:1550–6.

6. Keefe EB, Iwarson S, McMahon BJ, et al. Safety and immunogenicity of hepatitis A vaccine in patients with chronic liver disease. Hepatology 1998;27:881–6.
7. Magnani G, Falchetti E, Pollini G, et al. Safety and efficacy of two types of influenza vaccination in heart transplant recipients: a prospective randomized controlled study. J Heart Lung Transplant 2005;24:588–92.
8. Chalasani N, Smallwood G, Halcomb J, et al. Is vaccination against hepatitis B infection indicated in patients waiting for or after orthotopic liver transplantation? Liver Transpl Surg 1998;4:128–32.
9. Rytel MW, Dailey MP, Schiffman G, et al. Pneumococcal vaccine immunization of patients with renal impairment. Proc Soc Exp Bio Med 1986;182:468–73.
10. Linnemann CC Jr, First MR, Schiffman G. Response to pneumococcal vaccine in renal transplant and hemodialysis patients. Arch Intern Med 1981;141:1637–40.
11. Loinaz C, de Juanes JR, Gonzalez EM, et al. Hepatitis B vaccination results in 140 liver transplant recipients. Hepatogastroenterology 1997;44:235–8.
12. McCashland TM, Preheim LC, Gentry MJ. Pneumococcal vaccine response in cirrhosis and liver transplantation. J Infect Dis 2000;181:757–60.
13. Miyairi I, Funaki T, Saitoh A. Immunization practices in solid organ transplant recipients. Vaccine 2016;34:1958–64.
14. Broyer M, Tete MJ, Guest G, et al. Varicella and zoster in children after kidney transplantation: long-term results of vaccination. Pediatrics 1997;99:35–9.
15. McGregor RS, Zitelli BJ, Urbach AH, et al. Varicella in pediatric orthotopic liver transplant recipients. Pediatrics 1989;83(2):256–61.
16. Kaplan LJ, Daum RS, Smaron M, et al. Severe measles in immunocompromised patients. JAMA 1992;267(9):1237–41.
17. Danziger-Isakov L, Kumar D, the American Society of Transplantation Infectious Disease Community of Practice. Vaccination in solid organ transplantation. Am J Transplant 2013;13:311–7.
18. Kimball P, Verbeke S, Flattery M, et al. Influenza vaccination does not promote cellular or humoral activation among heart transplant recipients. Transplantation 2000;69:2449–51.
19. White-Williams C, Brown R, Kirklin J, et al. Improving clinical practice: should we give influenza vaccinations to heart transplant patients? J Heart Lung Transpl 2006;25:320–3.
20. Recommended immunization schedule for adults aged 19 years or older, United States, 2018. CDC.gov. Available at: https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf. Accessed January 1, 2018.
21. What everyone should know about Zostavax. CDC.gov. 2018. Available at: https://www.cdc.gov/vaccines/vpd/shingles/public/zostavax/index.html. Accessed February 19, 2018.
22. Smith CK, McNeal MM, Meyer NR, et al. Rotavirus shedding in premature infants following first immunization. Vaccine 2011;29:8141–6.
23. People at risk for foodborne illness - transplant recipients. FDA.gov. 2017. Available at: https://www.fda.gov/Food/FoodborneIllnessContaminants/PeopleAtRisk/ucm312570.htm. Accessed January 1, 2018.
24. Drinking water. CDC.gov. 2017. Available at: https://www.cdc.gov/healthywater/drinking/index.htm. Accessed January 14, 2018.
25. Food safety for transplant recipients. FDA.gov. 2011. Available at: https://www.fda.gov/downloads/Food/FoodborneIllnessContaminants/UCM312793.pdf. Accessed January 14, 2018.

26. Avery RK, Lonze BE, Kraus ES, et al. Severe chronic norovirus diarrheal disease in transplant recipients: clinical features of an under- recognized syndrome. Transpl Infect Dis 2017;19:e12674.
27. Foodborne illnesses and germs. CDC.gov. 2017. Available at: https://www.cdc.gov/foodsafety/foodborne-germs.html. Accessed January 14, 2018.
28. Trevejo RT, Barr MC, Robinson RA. Important emerging bacterial zoonotic infections affecting the immunocompromised. Vet Res 2005;36:493–506.
29. Healthy pets healthy people – organ transplant recipients. CDC.gov. 2014. Available at: https://www.cdc.gov/healthypets/specific-groups/organ-transplant-patients.html. Accessed January 15, 2018.
30. Kotton CN. Zoonoses in solid-organ and hematopoietic stem cell transplant recipients. Clin Infect Dis 2007;44:857–66.
31. Traveler's health. Chapter 8 – Advising travelers with specific needs. CDC.gov. 2017. Available at: https://wwwnc.cdc.gov/travel/yellowbook/2018/advising-travelers-with-specific-needs/immunocompromised-travelers. Accessed January 20, 2018.
32. Boggild AK, Sano M, Humar A, et al. Travel patterns and risk behavior in solid organ transplant recipients. J Travel Med 2004;11:37–43.
33. Ryan ET, Wilson ME, Kain KC. Illness after international travel. N Engl J Med 2002;347:505–16.
34. Held TK, Weike T, Mansmann, et al. Malaria prophylaxis: identifying risk groups for non-compliance. Q J Med 1994;87:17–22.
35. Behrens RH, Curtis CF. Malaria in travelers: epidemiology and prevention. BMJ 1993;49:363–81.
36. Patel RP, Liang SY, Koolwal SY, et al. Travel advice for the immunocompromised traveler: prophylaxis, vaccination, and other preventive measures. Ther Clin Risk Manag 2015;11:217–28.
37. Freedman DO, Weld LH, Kozarsky PE, et al. GeoSentinal surveillance network: spectrum of disease and relation to place of exposure among Ill returned travelers. N Engl J Med 2006;354(2):119–30.