Immunization of Solid Organ Transplant Candidates and Recipients: A 2018 Update

Christian Donato-Santana, MD,
Nicole M. Theodoropoulos, MD, MS*

KEYWORDS

• Vaccine • Immunization • Solid organ transplant • Immunosuppressed

KEY POINTS

- Appropriate vaccines should be administered as early in the pretransplant period as possible.
- Data are lacking regarding the safety of live vaccines in the posttransplant period and are currently contraindicated.
- Vaccines should be given before foreign travel, but yellow fever vaccine is currently contraindicated posttransplantation.

INTRODUCTION

Vaccination in transplant candidates is important, but often overlooked. Vaccine-preventable diseases continue to be a considerable cause of morbidity and mortality in solid organ transplant (SOT) candidates and recipients.[1] Vaccinating SOT candidates pretransplant can improve their posttransplant response to vaccines.[2] Certain vaccines may allow SOT recipients to accept organs they may not have otherwise, as in the case of the hepatitis B core antibody positive donor organs. In addition, in the case of influenza vaccine in particular, vaccination may help avoid organ turndown due to SOT candidate illness.

Ideally, SOT candidates should have their vaccines updated as early as possible before transplantation because vaccine immune response is decreased during organ failure and even more so in the setting of immunosuppression after transplant surgery. It is recommended to make sure measles, mumps, rubella, varicella, tetanus-diphtheria-pertussis, pneumococcal, influenza, and hepatitis A and B

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Division of Infectious Diseases & Immunology, University of Massachusetts Medical School, 55 Lake Avenue North, S7-715, Worcester, MA 01655, USA
* Corresponding author. Division of Infectious Diseases, University of Massachusetts Memorial Medical Center, 55 Lake Avenue North, S7-715, Worcester, MA, 01655.
E-mail address: nicole.theodoropoulos@umassmemorial.org

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vaccines are up to date in all appropriate candidates. If a patient has plans for foreign travel after transplant, it should be ensured that travel-related vaccines, especially live vaccines, are given before transplantation.

There is not a clear consensus about when vaccination should resume after transplantation although many centers vaccinate 3 to 6 months after transplantation. Serologic tests can be used to decide if certain vaccines are necessary pretransplant and should be used in certain instances to assess adequate immunologic response more than or equal to 4 weeks after vaccine administration.[3]

MECHANISMS OF IMMUNOSUPPRESION

It is important to understand the mechanism of immunosuppression in SOT recipients because this can help determine the appropriate timing of the vaccines. The immunosuppressive medications used in SOT recipients reduce B-cell and T-cell immune responses, which decrease the vaccine immune response.[4–7] Vaccine response is inversely proportional to the number of immunosuppressive drugs used.[7,8] Also, the specific immunosuppressive drug used may affect the level of immune response to vaccines. Previous studies have found that mycophenolate use was associated with decreased seroresponse in influenza-vaccinated kidney transplant recipients.[1,9,10] Another study evaluated the response to influenza vaccine in the setting of anti–T-cell therapy impact and did not find a significant difference with thymoglobulin versus basiliximab.[1,11]

TIMING

The current recommendation is to complete updating vaccines at least 4 weeks before transplant.[7,12–14] The American Society of Transplantation Third Edition of the Infectious Disease Community of Practice guidelines recommend at least a period of 4 weeks to repeat serologies after vaccine administration to ensure appropriate seroresponse.[3] Because patients are generally under the highest level of immunosuppression in the first 6 months after transplantation, it is recommended to avoid vaccinations in this period because of a likely lack of response. Patients are also recommended to avoid foreign travel in the early posttransplant period. After 6 months, immunosuppression can be reduced in some cases,[15] and therefore, there is improved immunogenicity and response to vaccination.[3,14] However, if T-cell depleting induction immunosuppression is used (ie, alemtuzumab or antithymocyte globulin), SOT recipients will have severely suppressed immune systems for up to 2 years posttransplantation.[16,17]

Several studies have been performed looking for antibody titers after exposure to monoclonal antibody medications. A study looking at vaccine response in patients with immune thrombocytopenia receiving rituximab after the *Haemophilus influenzae* type b (Hib) conjugate vaccine and the pneumococcal polysaccharide vaccine found that 3/14 (21%) in the rituximab group and 4/6 (67%) in the placebo group achieved a 4-fold increase of titers in antipneumococcal antibodies. On the other hand, 4/14 (29%) and 5/6 (83%) achieved a 4-fold increase for anti-Hib antibodies. This finding showed that the antibody responses were impaired for at least 6 months after rituximab administration.[18] A study on autologous hematopoietic cell transplant recipients showed that live vaccines (measles, mumps, and rubella virus [MMR] and Herpes zoster vaccine) were safe and well tolerated 24 months after transplant on patients with bortezomib maintenance therapy.[19] The use of plasma exchange could also affect antibody titers after vaccination. Renal transplant patients who received plasma

exchange sessions were found to have a decrease in antimeasles antibody titers from a mean of 3238 mU/l to a mean of 1710 mU/l, but after a median follow-up of 64 days the titers returned to baseline levels.[20]

LIVE, ATTENUATED VIRUS VACCINES

The most common live, attenuated virus vaccines (LAAV) include intranasal influenza (not recommended for use in the 2017–2018 influenza season), varicella zoster, herpes zoster, measles, mumps, rubella, rotavirus, yellow fever, oral polio, and Japanese encephalitis vaccines. The current recommendation is that all live vaccines must be given in the pretransplantation period, at least 4 weeks before transplantation. To facilitate the administration, live-attenuated vaccines can be administered on the same day with inactivated vaccines, and 2 live-attenuated vaccines can be administered on the same day; otherwise, the live vaccines need to be spaced 28 days apart.[3] The infusion of blood products or intravenous immunoglobulin can interfere with the response to LAAV, and therefore, it is recommended to delay vaccines for 3 months after blood products.[14] In addition, tuberculin skin test response may be rendered falsely negative by live vaccines[21] and for that reason is recommended to perform this test before or on the same day of LAAV, but not within 4 weeks of LAAV.[3] Ultimately, it is important to vaccinate as early as possible in the transplant evaluation period.

It is thought that LAAV are unsafe to administer in the setting of immune suppression, and therefore, post-transplant live vaccines are not recommended. There were prospective studies evaluating pediatric SOT recipients who received varicella or MMR vaccines and no adverse events were reported. There was also a retrospective study in Brazil of 19 SOT recipients who received yellow fever vaccine without adverse outcome.[3,22]

A recent study evaluated SOT recipients who received LAAV to look for a correlation between the vaccine and organ rejection. Three cases of organ rejection were found; 1 patient showed chronic rejection at the time of vaccination, 1 patient had a rejection episode of the liver more than 1 year after the varicella vaccine, and 1 patient had acute organ rejection 3 weeks after measles vaccination.[23] The investigators concluded receipt of LAAV did not increase rates of organ rejection in SOT recipients.[23–26]

SOT recipients should use prevention precautions with family members who have received the rotavirus vaccine. This would include avoiding diaper changing in the infant recipient of the vaccine or frequent hand washing after changing diapers in an infant (if unable to avoid diaper changing), and these precautions should be continued for a period of at least 2 weeks after administration of the vaccine.[3,27] The shedding of the virus may occur up to 1 month after the last dose.[28–30] SOT recipients also need to avoid close contact with household contacts who have received the oral polio vaccine (which is no longer available in the Western Hemisphere). The Infectious Diseases Society of America (IDSA) clinical practice guideline recommends against using the live attenuated oral polio vaccine in persons who live with immunocompromised hosts.[14] Rare cases of vaccine-associated paralytic poliomyelitis have been reported. The transmission of the virus after vaccination is by shedding in the stool.[14,31,32] Otherwise, there are no additional precautions recommended if household contacts receive other live vaccines.

MEASLES, MUMPS, AND RUBELLA VIRUS VACCINE

During transplant evaluation, studies should include MMR serologies, especially if the status of vaccination or previous infection is unknown. The MMR is a live, attenuated vaccine and is only recommended to be administered before transplant but have been administered in selected organ transplant recipients on minimal immunosuppression.[3,33]Adult

patients could receive a second dose of MMR if there is no seroconversion by 4 weeks. In a recent article, the only reported adverse effect with the mumps immunization in immunosuppressed patients was transient swelling of the parotid glands.[23]

MMR vaccine administration in pediatric patients is recommended before transplant but the infant must be younger than 6 months; a second dose will be needed if the infant did not receive a transplant before 1 year of age.[3,34–38] A study of pediatric recipients of living donor liver transplantation evaluated the safety and effectiveness of MMR vaccination and the patients achieved seroconversion for the live, attenuated strains of measles, mumps, and rubella administered separately and there was no evidence of infection after the immunization.[1,39] At this time, the MMR vaccine is contraindicated after transplantation due to insufficient data about safety and the concern for the development of vaccine-acquired disseminated infection without available effective treatment.[14]

VARICELLA ZOSTER "CHICKEN POX" VACCINE

Transplant patients are at high risk for severe complications from varicella zoster virus (VZV) infection and for that reason pretransplant serologic studies should include VZV immunoglobulin G antibody titers. Seronegative organ transplant candidates should be offered the varicella vaccine more than 4 weeks before transplantation.[14] However, if an otherwise appropriate organ is offered within this 4-week period, it should be accepted, because prophylactic antiviral agents including acyclovir or valganciclovir would be effective in "turning off" this vaccine, thus effectively preventing vaccine-associated disseminated infection. The varicella vaccine is a live, attenuated vaccine and in adults only 1 dose is needed. A second dose could be administered if the patient does not seroconvert 4 weeks after administration.[3,40–43] The varicella vaccine also can be administered in a 2-dose strategy for patients older than or equal to 13 years, separated by 4 weeks between doses; in patients aged between 1 and 12 years old, greater than or equal to 3 months separation is recommended.[14]

In posttransplant patients, a vesicular rash has been reported after varicella vaccine administration in 2 separate pediatric studies.[1,43,44] The Weinberg study noted an 87% VZV seroconversion rate with a single-dose approach, whereas Posfay-Barbe and colleagues observed that 7 of 32 of children required a third dose of varicella vaccine to achieve seroconversion.[1,43,44] Although LAAV are generally contraindicated post-transplantation, the IDSA guidelines make an exception for seronegative pediatric liver and kidney transplant recipients, because they have a high risk of primary varicella infection.[14] A recent article reported 14/339 SOT transplant recipients had a varicella vaccine-related infection and it was of moderate severity, defined as skin manifestations without complications.[23,43,45,46]

HERPES ZOSTER "SHINGLES" VACCINE

Herpes zoster (HZ) is often seen in SOT recipients, putting them at risk for the complications of postherpetic neuralgia, bacterial superinfection, disseminated disease, and death.[1,47] All SOT candidates should receive HZ vaccine more than 4 weeks before transplantation, but, as with varicella vaccine, if an otherwise appropriate organ is offered within this 4-week period, it should be accepted, as patients will be typically given a prophylactic antiviral post-transplant. Despite the increased risk of these complications posttransplant, the currently available HZ vaccine continues to be contraindicated after transplant because there is a theoretical risk of vaccine-derived HZ and a lack of safety and efficacy data in these patients.[14] A new nonlive recombinant subunit HZ vaccine was approved in the United States as of October 2017.[48] There are

currently no data in SOT recipients, but theoretically, given that the new vaccine is not live, it may be preferred in this patient population, including in patients who previously received the live, attenuated HZ vaccine. More data are needed before this can be formally recommended.

INFLUENZA VIRUS VACCINE

The standard dose intramuscular vaccine has been studied the most in SOT recipients. Because of the seasonal nature of influenza, patients are often in the first 6 months posttransplant during influenza season and there is a concern that they will have a decreased immune response to the vaccine. A review article in 2013 demonstrated that although administering the influenza vaccine in the first 6 months after transplant results in poor immunologic response, it was still effective in preventing clinical influenza.[49] A multicenter cohort study in 2015 demonstrated (contrary to common belief) that the time from transplantation had no association with response to vaccination.[50] These 2 studies support the importance of the influenza vaccine in transplant patients, even in the early posttransplant period. A multicenter prospective cohort study showed that the influenza vaccine is safe after SOT and reported 1/798 patients developed renal transplant rejection. That patient had an increasing trend in serum creatinine before the vaccine and was diagnosed previously with chronic rejection making the rejection associated to vaccination unlikely.[50] In addition, a randomized trial of 60 kidney transplant recipients compared the safety and immunogenicity of adjuvanted versus nonadjuvanted influenza vaccine and they did not find an increase in human leukocyte antigen alloantibodies in patients who received the adjuvanted vaccine.[51] In the event of a vaccine shortage, intradermal administration of a smaller dose of influenza vaccine is appropriately immunogenic.[52]

In studies evaluating the outcome of a single-dose versus a two-dose booster vaccine, those that received the booster vaccine have higher titers at 10 weeks than those that received a single dose, but there is no difference after 1 year, and no difference in efficacy in preventing clinical influenza.[53] A clinical trial in 2014 by Felldin and colleagues[5] demonstrated an increase in antibody titers after a yearly booster. In pediatric patients, a double-blind study was performed using a high-dose versus standard dose of an inactivated trivalent vaccine and they showed increased immunogenicity with the high-dose vaccine.[54] Revaccination in 3 to 6 months within the influenza season is also a reasonable approach.[3]

Recently a double-blind randomized trial study was published, which compared the high-dose vaccine (Fluzone HD, Sanofi Pasteur, Swiftwater, PA) and the standard dose vaccine (Fluviral, GlaxoSmithKline, Mississauga, ON) in SOT recipients. In the study, the high-dose vaccine had superior immunogenicity for all the virus strains (A/HINI, A/H3N2, and B/Brisbane). The study also evaluated safety and reported no significant differences in local adverse events. This study suggests the possibility of providing the high-dose vaccine in SOT recipients instead of the standard dose.[55]

Live, attenuated influenza vaccines have been studied in patients with HIV and cancer and have been shown to be safe, but studies are lacking in SOT recipients.[3,56,57]

HUMAN PAPILLOMAVIRUS VIRUS VACCINE

There are limited data regarding the human papillomavirus virus (HPV) vaccine in SOT recipients. However, the HPV vaccine series is important to consider because there is an increased risk of anogenital HPV-associated neoplasia in SOT recipients.[1,58,59] If the vaccine is given, it should be administered previous to the transplantation and consists of 3 doses. If it is not possible to complete the schedule before the

transplantation, the vaccine schedule could be resumed 3 to 6 months after transplant. One study evaluated the immune response to the HPV vaccine in posttransplant patients and it found that the vaccine is safe, but immunogenicity was suboptimal.[3,60]

PNEUMOCOCCAL VACCINE

SOT recipients have a high rate of morbidity from pneumococcal disease (*Streptococcus pneumoniae* infection), and therefore, the pneumococcal vaccine is recommended by the IDSA clinical practice guideline for vaccination of the immunocompromised host.[1,14,61] Adults and pediatric transplant recipients older than or equal to 6 years should receive 1 dose of the 13-valent protein-conjugate vaccine (PCV-13) followed at least 8 weeks later by the 23-valent polysaccharide vaccine (PPSV-23).[1,62,63]

Children younger than 2 years should receive the PCV-13 vaccine according to the Advisory Committee on Immunization Practices (ACIP) recommendations depending on the age.[64] Children aged 24 to 71 months should receive the PCV-13 depending on the previous doses (**Table 1**). Children older than 5 years should receive the PPSV-23.[3,64]

In adult posttransplant patients, the PCV-13 vaccine produces a similar immune response as the PPSV-23,[3,65] although one randomized study on adult liver transplant recipients showed that there is no additional benefit for the serotypes contained in the PCV-13 by giving the PPSV-23 8 weeks later[3,66]; an immunization strategy known as "prime-boost" is still recommended.

In adult patients who received more than or equal to 1 dose of PPSV-23, PCV-13 should be administered more than or equal to 1 year after the last dose of PPSV-23. In pediatric patients the recommendation is to administer PCV-13 more than or equal to 8 weeks after the last dose of PPSV-23.[1,63] There are some data supporting annual monitoring of pneumococcal titers because they have been reported to decline.[3,61] However, there are currently no specific recommendations to guide interpretation of these titers in SOT candidates or recipients and when to revaccinate.

TETANUS, DIPHTHERIA, PERTUSSIS VACCINES

Diphtheria, tetanus, pertussis (DPaT or Tdap) vaccine is recommended to be administered before SOT because it is safe and immunogenic in patients with end-stage liver disease and end-stage renal disease.[7,67,68] SOT patients should receive a tetanus booster 5 years after last administration.[7,69] Adults should receive one Tdap followed by Td boosters every 10 years.

ROTAVIRUS VACCINE

The rotavirus vaccine has not been studied well in transplant patients and at this moment the vaccine is not listed as a contraindication because there have not been

Table 1
Summary of pneumococcal vaccine recommendations in children aged 24–71 mo

Previous Dose	Schedule[3,59]
Unvaccinated	2 doses of PCV-13
Incomplete schedule of 3 doses	2 doses of PCV-13, first dose ≥8 wk after most recent dose, second dose ≥8 wk later
4 doses of PCV 7 or other age-appropriate schedule	1 dose of PCV-13, ≥8 wk after most recent dose

reports of vaccine-derived rotavirus infection.[1,28] If an infant in a transplant recipient's household receives the vaccine, the transplant recipient should avoid contact with diapers and stool for 4 weeks after each vaccine administration.[14]

HEPATITIS A VIRUS VACCINE

Hepatitis A virus (HAV) vaccine is recommended before liver and intestinal transplantation and is an important vaccine for foreign travelers. SOT patients need 2 doses of the vaccine to have an adequate antibody response.[7,70] The seroconversion after one dose of HAV vaccine in SOT recipients was found to be 41% in liver transplants and 24% in renal transplants recipients. When a second dose of the vaccine is received the data showed that the seroconversion increases to 97% in liver transplant and 72% in renal transplant recipients.[7,8] In some cases, a booster dose can be considered because the antibody response has been shown to wane by 2 years postvaccination in the SOT population.[7,71]

HEPATITIS B VIRUS VACCINE

Hepatitis B virus (HBV) vaccine is recommended before transplantation in all cases, given the potential for HBV transmission from blood and/or organ donors. The efficacy of repeated HBV vaccination ranges from 32% to 36% in SOT recipients compared with 90% to 95% in healthy controls.[7,72–74] Transplant candidates with liver cirrhosis who receive accelerated HBV vaccine regimen have lower vaccine response rates than patients without liver cirrhosis.[1,75,76] The United States Centers for Disease Control and Prevention (CDC) and IDSA recommend that adult immunocompromised patients receive the higher (40 μg) dose of HBV vaccine.[7,14,77] Vaccine titers should be measured at least yearly to ensure ongoing protective immunity (hepatitis B surface antibody >10 unit/mL).[3]

VACCINES FOR SPECIAL SITUATIONS

During intraabdominal transplant surgery, particularly multivisceral transplantation, occasionally there is injury to the spleen requiring splenectomy. Also, some SOT candidates have had splenectomies in the past for other reasons. The current recommendations are to ensure meningococcal, Hib, and pneumococcal vaccines are up to date before (if possible) or after splenectomy. The pretransplantation evaluation should identify patients with asplenia or those planning to undergo splenectomy. Development of atypical hemolytic uremic syndrome or recipients of human leukocyte antigen or ABO incompatible donor organs may also benefit from these vaccinations. The patients under these circumstances should receive meningococcal, Hib, and pneumococcal vaccines. According to the CDC, both the meningococcal conjugate vaccine and the meningococcal serogroup B vaccine should be administered for *Neisseria meningitidis* protection in asplenic patients.[30] In patients older than or equal to 10 years with persistent complement deficiencies, patients taking eculizumab, or those at increased risk from serogroup B meningococcal disease outbreak, ACIP recommends the meningococcal serogroup B vaccine in addition to the meningococcal conjugate vaccine.[1,30,78] For Hib protection, transplant candidates or recipients with asplenia should receive a 1-time dose of Hib conjugate vaccine.[30]

Patients who are traveling to *N. meningitidis* endemic areas should receive a meningococcal vaccine. A 2015 study by Wyplosz and colleagues evaluated the immunogenicity of quadrivalent meningococcal vaccine in SOT recipients. The study

showed that 2 of 5 patients developed seroprotective titer (hSBA $\geq$4) for the MenC serogroup with the nonconjugate vaccine. With the conjugate vaccine, 6 of 10 patients had protective meningococcal titers, but only 1 developed a booster response (a 4-fold increase in hSBA titers) and only for the MenC serogroup.[79] This study demonstrates a low immune response to the quadrivalent meningococcal vaccine in SOT recipients but because it does provide some seroprotection to patients at risk, the recommendations remain to administer the vaccine when indicated in SOT recipients.

VACCINES FOR TRAVEL OUTSIDE THE UNITED STATES

Transplant recipients can receive travel vaccines but the schedule should be individualized to the area visited and the increased risk of infection for that area.

The *inactivated polio virus vaccine (IPV)* response rates in renal transplant patients were comparable to healthy individuals.[80] If the patient is planning to travel to a polio endemic region, he/she is recommended to have a booster dose of IPV every 10 years.[7,81] The live, attenuated oral polio vaccine should be avoided in post-SOT patients and their household contacts.

Cholera vaccines have been used to reduce diarrhea rates in healthy travelers going to areas of *Vibrio cholerae* outbreaks, but the efficacy data in immunocompromised hosts are limited.[7,82] The live, attenuated form should be avoided in SOT recipients, but the inactivated form may be considered for travel to cholera endemic and outbreak areas.

Patients going to *Japanese encephalitis virus* endemic areas should receive this inactivated vaccine if they will be in high-risk locations or have a prolonged trip to the area. There are limited data for vaccine efficacy in the SOT population. Accelerated regimens or boosting with 2 doses (days 0 and 28) in SOT recipients are recommended with a booster every year for high-risk travelers.[7,13,83–85]

There are case reports of successful *rabies virus* inactivated vaccine preexposure prophylaxis in renal transplant and pediatric SOT recipients.[86–88] The recommendation for preexposure prophylaxis is a 3-dose regimen (days 0, 7, and 28) for high-risk travelers.[89] Postexposure prophylaxis is recommended in transplant recipients who are discovered retrospectively to have unexpectedly received organs from rabies-infected donors with a 5-dose schedule recommended (days 0, 3, 7, 14, and 28)[90] in conjunction with immunoglobulin depending on the category of exposure.[7,89]

In case an SOT patient needs to receive the *typhoid fever vaccine* for *Salmonella typhi* before travel to an endemic country, the inactivated Vi polysaccharide vaccine is preferred to the oral live, attenuated vaccine.[13] The greatest risk area for travelers is South East Asia.[7,91] A single dose of the vaccine confers protection for 2 years and a booster should be given every 2 years to patients at risk.[1,92]

Yellow fever virus vaccine before SOT can have prolonged seropositivity posttransplantation. In one study, protective antibody level was detectable in 52 of 53 patients.[93] A retrospective review published in 2012 of 19 SOT patients who received the live, attenuated yellow fever vaccine posttransplant did not show any significant side effects.[94] Death has been reported after vaccine administration in immunosuppressed individuals in the past due to viscerotropic and neurotropic vaccine–related disease and for that reason it remains contraindicated after SOT.[7,95] SOT recipients will need a physician note to excuse them from the vaccine in order to enter certain countries that require vaccination for entrance.

Table 2
Summary of vaccine recommendations for solid organ transplant candidates or recipients

Vaccine	Inactivated/ Live Attenuated (I/LA)	Candidates	Dose	Timing	Monitor Vaccine Titers	Comments
MMR	LA	Seronegative for ≥1 of the 3 viruses, especially for measles or mumps	1–2 doses	• 4 wk before transplant	Yes	Check for seroresponse >4 wk after vaccine
Varicella	LA	Seronegative for VZV	1–2 doses	• 4 wk before transplant	Yes	Check for seroresponse >4 wk after vaccine
Herpes Zoster	LA	Aged ≥50 y regardless of VZV immunity	1 dose	• 4 wk before transplant	No	New inactivated vaccine approved in October 2017
Influenza	I	All candidates	1 dose	Before Influenza season	No	Consider the high-dose formulation
HPV	I	Ages 9–26 y	3 doses	Before or after transplant	No	
Pneumococcal PPSV-23	I	All candidates if ≤2 doses in the past	Every 5 y	Before or after transplant	No	
Pneumococcal PCV-13	I	All candidates if not yet received	1 lifetime dose (give 1 y after last PPSV-23 dose)	Before or after transplant	No	
DPaT/Tdap	I	All candidates if not previously received	Every 7–10 y	Before or after transplant	No	

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Table 2
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Vaccine	Inactivated/ Live Attenuated (I/LA)	Candidates	Dose	Timing	Monitor Vaccine Titers	Comments
Inactivated polio	I	All candidates if not previously received; one booster dose recommended to adults traveling to endemic areas	3 doses to children or unvaccinated adults	Before or after transplant	No	
Cholera (CVD 103-HgR)	LA	Candidates traveling to endemic areas or outbreaks	1 dose	Before transplant only if high-risk travel	No	There are no safety or efficacy data in immunosuppressed patients There are inactivated oral cholera vaccines available directly from the manufacturer
Japanese encephalitis	I	Candidates traveling to endemic areas for >1 mo or <1 mo in areas of increased transmission	2 doses at 0 and 28 d	Before or after transplant	No	
HAV	I	Seronegative for anti-HAV	2 doses at 0 and 6 mo	Before or after transplant	Yes	Recommended for foreign travel or before liver or intestinal transplant
HBV	I	Seronegative for anti-HBs	3 doses at 0, 1 and 6 mo	Before or after transplant	Yes	
Rabies	I	High-risk travelers defined by WHO[a]	3 doses at 0, 7, and 21 or 28 d	Before or after transplant	No	Postexposure 5 doses at 0, 3, 7, 14, and 28, plus rabies immunoglobulin
Typhoid fever	LA or I	Candidates traveling to endemic areas	1 dose	Before or after transplant	No	Use inactivated vaccine only after transplant

Yellow fever	LA	Candidates traveling to endemic areas	1 lifetime dose	Before transplant	No	Posttransplant patients will require medical note to enter certain countries without vaccine because it is contraindicated after transplant
Meningococcal conjugate (MenACWY and MPSV4)	I	Candidates with asplenia, college students, and military personnel	2 doses, 8 wk apart	Before or after transplant	Yes	Every 3 y as needed depending on titers
Serogroup B meningococcal	I	Candidates aged ≥10 y with persistent complement deficiencies, patients taking eculizumab, or those at increased risk from serogroup B meningococcal disease outbreak	MenB-FHbp: 3 doses MenB-4C: 2 doses	Before or after transplant	Yes	Asplenic patients should receive both the meningococcal conjugate and serogroup B vaccines
Hib	I	Candidates with asplenia	1–2 doses separated by 4–8 wk	Before or after transplant	Yes	Measuring titers at least once may be helpful

Abbreviation: WHO, World Health Organization.

[a] Candidates at high risk are those who will be at increased risk of exposure to rabies virus (eg, laboratory workers dealing with the virus, veterinarians, and animal handlers). Other group that is at high risk includes travelers with extensive outdoor exposure in rural high-risk areas where immediate access to appropriate medical care may be limited.[84]

SUMMARY

A vaccination protocol pretransplantation is the best way to provide all the needed vaccines to an SOT candidate or recipient (**Table 2**). The recommendation is to complete all necessary vaccines before transplantation, ideally at least 4 weeks before transplantation, because after transplantation the immunosuppressive therapy will decrease the vaccine immune response. Live, attenuated vaccines remain contraindicated after transplantation, but inactivated vaccines can be given after transplant safely. The optimal timing to begin posttransplant vaccination is 6 months after transplantation but should be individualized for each patient. Additional vaccines are required for SOT candidates or recipients with asplenia, persistent complement deficiencies, or at increased risk for meningococcal disease (college students, military personnel, and during outbreaks). In those scenarios, the SOT candidates and recipients should receive the meningococcal and Hib vaccines. An individualized evaluation should be done in travelers to foreign countries according to each patient's risks. In conclusion, the current evidence favors the use of live, attenuated vaccines before transplantation, and the inactivated vaccines could be safely used before or after transplantation.

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