

Principles of Immunization for Hematopoietic Stem Cell Transplant (HSCT) and Solid Organ Transplant (SOT) Recipients

Revision Date: July 18, 2023

These recommendations do not impose mandatory immunization requirements on transplant recipients, and are not intended to replace the clinical skill, judgement and decisions of the individual's transplant healthcare team. These recommendations are meant to supplement existing recommendations for routine immunization as outlined in the current [Alberta Immunization Policy](#).

General Principles

1. This is a high-risk population. HSCT recipients are at a significant risk of infection after transplant and prior to immune reconstitution. SOT recipients have a higher lifetime risk of severe infections due to their immunosuppressive regimens.
2. Existing vaccine contraindications should be followed.
3. Wherever possible, schedules consistent with the Canadian Immunization Guide¹ and Alberta Health Immunization Policy were followed in the development of these recommendations. Where these recommendations differ from the CIG they are based on expert review and expert opinion. The recommendations are intended to supplement the practices outlined in the current Alberta Immunization Policy. Discussion between public health staff, the Medical Officer of Health and the transplant physician may be required to clarify schedules commenced at specific ages.
4. A decreased response to immunization in this population is expected post-transplant.
5. Repeat immunizations/multiple doses may be necessary to ensure immunity.
6. Vaccines should be administered prior to planned immunosuppression if feasible.^{1,2}
 - a. Live vaccines* should be administered at least four weeks prior to immunosuppression and 4 weeks prior to transplant.³ This is rarely applicable to pre-HSCT patients as they are typically immunocompromised by the nature of their disease.

For those undergoing deceased donor organ transplant, if an organ becomes available in less than four weeks post-immunization, there is no contraindication to proceeding with the transplant.³
 - b. **Inactivated** vaccines should be administered at least two weeks prior to planned immunosuppression in order to allow for maximal response. For those undergoing deceased donor organ transplant, if an organ becomes available in less than two weeks post-immunization, there is no contraindication to proceeding with the transplant.
7. Assessment of immunity (antibody response) should be considered when a suitable laboratory test is available. This is more important in accelerated or altered schedules and in individuals with other high-risk exposures, such as health care workers.
 - a. The availability and utility of serological assessment has been reviewed by the Provincial Laboratory of Public Health (PLPH). Laboratory recommendations have been based on guidance from the PLPH.
 - b. Ordering the serology needed to assess the immunity following immunization and the interpretation of the serology results is the responsibility of the transplant physician. Patients identified, by their transplant healthcare team, as needing further immunization should be referred to Alberta Health Services/First Nations Inuit Health Branch.

***Live vaccines include:** BCG, LAIV (Flumist®), MMR, MMR-Var, oral polio, rotavirus, oral typhoid, varicella vaccine, varicella zoster vaccine: shingles (Zostavax®), yellow fever.

8. Household contacts and health care workers should be up-to-date for routine immunizations as per the Alberta Health immunization schedule, including annual influenza, to reduce the risk of disease transmission to transplant recipients. For live vaccines* the following precautions should be followed:
 - Varicella - If the vaccine recipient develops a varicella-like rash, the rash should be covered when possible; when not possible, direct contact with susceptible high-risk individuals should be avoided for the duration of the rash.¹
 - Rotavirus - may be administered to infants living in households with individuals who are immunocompromised. To minimize the risk of transmission of rotavirus vaccine virus, parents/caregivers should be counseled regarding the importance of hand washing particularly after diaper changes, before food preparation or direct contact with the immune compromised person.^{1,4}
 - Influenza - Individuals who have received FluMist® should avoid close association with individuals with severe immunocompromising conditions (e.g., bone marrow transplants recipients requiring protective isolation) for at least two weeks following immunization.⁵

Refer to specific Biological Products.

9. An assessment of immune competency should always be conducted by the attending physician prior to commencing immunization post-transplant.
10. Flexibility is necessary in interpreting the immunization recommendations. Clinical judgment and appropriate consultation (Medical Officer of Health, infectious disease experts, and transplant physicians) can assist with individualizing the patient's immunization plan when necessary. Patients, who are delayed beyond specified timelines in the recommendations should be offered an accelerated immunization schedule using minimum intervals between vaccine doses until caught-up to the regular schedule.
11. For the purposes of these recommendations, individuals younger than 18 years of age are considered children, and those 18 years of age and older are considered adults. However, where dosages/schedules are based on age (e.g., hepatitis B vaccine), recommendations from the product manufacturer should be followed unless specifically stated in the transplant protocols or related Alberta immunization policies.
12. We recommend the use of Alberta Immunization Policies for out-of-province patients returning to their home province for immunization. However, the most important objective is that the patient receives immunization or re-immunization as deemed necessary by the patient's transplant healthcare team. Alternate recommendations used by the patient's home province may be followed if needed to obtain this objective.

HSCT Principles

1. The recipient and donor immunization status pre-transplant both have an impact on post-transplant immunity. Immunity established prior to HSCT may increase immune response following transplant.
 - a. **Recipient:** Candidates should receive vaccines indicated for immunocompetent individuals based on age, immunization history and exposure history if they are not already immunosuppressed by the nature of their disease.^{1,2} Administer the appropriate inactivated vaccines or boosters at least two weeks prior to the transplant conditioning. live vaccines* should be administered at least four weeks prior to transplant.^{1,2,3} **Consult the attending transplant physician.**
 - b. **Donor:** The donor should be current with routinely recommended vaccines based on age, immunization history and exposure history. Administer routine inactivated vaccines or boosters at least two weeks prior to stem cell harvest. live vaccines* should be administered at least four weeks prior to the stem cell harvest.^{1,2} Additional immunization of the donor for the benefit of the recipient is not routinely recommended. **Consult the attending transplant physician.**
- Note:** Only routine vaccines are publicly funded for donors.
2. Regardless of pre-transplant immunization status, the recipient's immunity to vaccine-preventable diseases is decreased post-transplant. For this reason, it is recommended that most immunization schedules are started anew in HSCT recipients, **using the following schedules:** [Child HSCT](#) and [Adult HSCT](#).

*Live vaccines include: BCG, LAIV (Flumist®), MMR, MMR-Var, oral polio, rotavirus, oral typhoid, varicella vaccine, varicella zoster vaccine: shingles (Zostavax®), yellow fever.

3. The adult and pediatric schedules are very similar. They were developed separately to ensure that the appropriate combined vaccines are used for children.
4. Autologous HSCT involves the use of hematopoietic stem cells from the same person (i.e., the donor and the recipient are the same individual). Allogeneic HSCT involves two people: one donor and one recipient. There is no difference in recommended schedules between autologous or allogeneic recipients. Although a current topic of research, the differences in immunity post-transplant for the two types of recipients are not enough to justify two separate schedules.
5. The post-transplant period refers to the period of time the HSCT recipient is immunocompromised and is generally about 24 months. The majority of HSCT recipients will have a detectable antibody response to vaccine at six months post-transplant which continues to increase over the next 12 to 24 months. However, immune system recovery post-HSCT is variable and requires physician assessment. Graft versus host disease (GVHD), and the treatment thereof, prolongs the duration of immunosuppression.
6. Patients who are treated with rituximab, (or other B cell or T cell depleting antibodies), should have all their inactivated vaccines postponed until at least six months after the last dose of rituximab and live vaccines* postponed until at least 12 months after the last dose of rituximab.³ A clearance letter from the patient's transplant healthcare team is required before starting immunization.³
7. Patients who are treated with chemotherapy after transplant ("maintenance therapy") should also have all their immunizations postponed until at least six months after the last dose of chemotherapy. For new agents used for maintenance therapy (e.g. lenalinomide/revlimid), it is not known how they impact patients' ability to respond to vaccines; some physicians elect to have their patients immunized.³ A clearance letter from the patient's transplant healthcare team is required before starting immunization.³
8. HSCT recipients who have started their post-HSCT vaccine series and then had the series interrupted by Chimeric Antigen Receptor T (CAR) T-cell therapy are recommended to restart their vaccine series at least 6 months post CAR T-cell therapy (except for COVID-19 and inactivated influenza immunization which may be restarted as early as 3 months post CAR T-cell therapy)⁷.
9. The attending transplant physician should be consulted prior to administering any live vaccines*. Live vaccines* are administered at 24 months post-transplant to patients who no longer have GVHD and are off of immunosuppressive drugs. Live vaccine cannot be administered to patients with active GVHD, to patients on immunosuppressive medications (a wait period of at least three months after discontinuation of immunosuppressive drugs is recommended), to patients whose hematologic malignancy (e.g., leukemia) has relapsed or to patients who are for other reasons considered immunocompromised by the transplant physician.^{1,2}
10. If the HSCT recipient contracts varicella disease or shingles during the pre or post-transplant period, immunization with a varicella vaccine should still be provided as recommended.
11. Post-transplant patients should not receive live vaccines* if they relapse with underlying disease (typically leukemia) – in this scenario, live vaccines* could hasten death. Inactivated vaccines, particularly pneumococcal vaccine, should be considered in those with anticipated intermediate survival as assessed on a case-by-case with the transplant physician.
12. Patients who for whatever reason have not undergone the routine post-HSCT immunization schedule in the first three years post-transplant (e.g., patients who underwent HSCT before routine immunization of HSCT recipients in Alberta was recommended - approximately 2008) should be assessed as below:
 - a. If they are no longer on immunosuppressive drugs, immunization are recommended to start anew using recommendations for unimmunized individuals in the general population (e.g., diphtheria, tetanus, polio vaccine series, one dose of pertussis-containing vaccine, annual influenza vaccine and MMR if seronegative etc.).
 - b. If they are on immunosuppressive drugs, the patients are recommended to receive an accelerated post-HSCT immunization schedule (using the minimum intervals between vaccine doses). Live vaccines* are contraindicated for patients on immunosuppressive drugs until at least 3 months after discontinuation of all immunosuppressive drugs.³

***Live vaccines include:** BCG, LAIV (Flumist®), MMR, MMR-Var, oral polio, rotavirus, oral typhoid, varicella vaccine, varicella zoster vaccine: shingles (Zostavax®), yellow fever.

13. Travel vaccines, if needed, should be administered at two years post-transplant or later, as long as the patient has been off of immunosuppressive drugs for at least three months. This is an absolute requirement for live vaccines*. Non-live vaccines can be administered at 6 – 12 months; however, immunogenicity is limited, so waiting until 24 months or later is preferred. Live vaccines* including yellow fever are contraindicated in the first two years post-transplant. After that, live vaccines* can be administered if the patient does not have a relapse or active graft-vs-host disease, and if the patient is off immunosuppressive drugs. For travel vaccines, refer individuals to local travel health professionals.

SOT Principles

1. For the purpose of immunization, the following organs (or parts thereof) are considered solid organ transplants: heart, lung, kidney, liver, pancreas, small bowel and islet cells. These recommendations do not apply to skin, bone and cornea transplants since these are tissue transplants and do not require immunosuppression.
2. Immunization series' do not need to be restarted after SOT. Pre-transplant immunity is retained, although it may be reduced.
3. Prolonged/lifelong immunosuppression impacts vaccine efficacy post-transplant and increases the risk of using live vaccines*.
 - a. Generally, live vaccines* should not be considered for post-transplant patients.
 - b. If there is an inactivated vaccine available (e.g., when indicated for typhoid fever), it should be used in place of a live vaccine.
4. The priority is to ensure all potential SOT recipients are offered all recommended immunizations as soon as possible after they are identified and as early in the course of disease as possible because vaccine response may be reduced in people with organ failure pre-transplant.¹
5. Accelerated vaccine schedules should be used when necessary to ensure immunity in the recipient prior to transplant.
6. SOT recipients should be on **baseline** (maintenance) immunosuppression prior to restarting immunization series. This usually occurs from 6 to 12 months⁶ post-transplant and is best determined by the attending transplant physician.
7. Living donors should be up-to-date with routinely recommended vaccines based on age, immunization history and exposure history following recommendations below:
 - a. Administration of live vaccines* should be avoided within four weeks prior to organ donation.^{1,2}
 - b. Immunization of donors (other than routine immunization) solely for the recipient's benefit is generally not recommended.^{1,2}

See schedules for Solid Organ Transplant:

- [Child SOT \(Before 18 Months of Age\)](#)
- [Child SOT \(After 18 Months of Age\)](#)
- [Adult SOT](#)

***Live vaccines include:** BCG, LAIV (Flumist®), MMR, MMR-Var, oral polio, rotavirus, oral typhoid, varicella vaccine, varicella zoster vaccine: shingles (Zostavax®), yellow fever.

References

- ¹ National Advisory Committee on Immunization. (2016). *Canadian Immunization Guide* (Evergreen ed.). Ottawa, On: Public Health Agency of Canada. www.canada.ca/en/public-health/services/canadian-immunization-guide.html
- ² Rubin, L. G., et al. (2014, February). 2013 IDSA clinical practice guidelines for vaccination of the immunocompromised host. *Clinical Infectious Diseases*, 58(3). 309-318
- ³ Expert opinion of Alberta HSCT Program physicians (2017, September).
- ⁴ GlaxoSmithKline Inc. (2014, February 21). ROTARIX®: Human rotavirus, live, attenuated, oral vaccine. *Product Monograph*.
- ⁵ National Advisory Committee on Immunization. (2016). Statement on seasonal influenza vaccine for 2016-2017. Retrieved November 3, 2017 from: <https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/naci-ccni/assets/pdf/flu-2016-2017-grippe-eng.pdf>
- ⁶ Expert opinion of Alberta Solid Organ Transplant Program physicians (November 2027 and November 2019).
- ⁷ Expert opinion of Alberta Hematopoietic Stem Cell Transplant Program physicians (May 2022).