Cancer Care Ontario

Immunization Following Stem Cell Transplant in Adults: Position Statement

Stem Cell Transplant Steering Committee

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Objective

To harmonize post-transplant immunization recommendations for patients undergoing autologous or allogeneic hematopoietic stem cell transplantation.

Summary of Recommendations

1. Certain live vaccines can be administered at least 24 months after transplant, including univalent varicella, MMR and yellow fever (see precautions below). Other live vaccines are not recommended. Varicella and MMR immunity can be checked at 24 months to see whether the vaccines are truly needed or not.

2. Inactivated vaccines may be started as early as 3 months post-transplant. Table 1 summarizes the recommendations for inactivated vaccines.

3. Autologous transplant recipients may not require full re-vaccination compared with allogeneic transplant recipients. Serological testing for Hepatitis A and B, measles, mumps, rubella, varicella and tetanus are available (see references for link to requisition) and can be done prior to vaccination.

4. Close contacts should ensure their vaccinations are up to date. If non-immune, either through previous infection or immunization, close contacts should be vaccinated using appropriate precautions, against measles-mumps-rubella (MMR), varicella or zoster, and routinely against influenza, hepatitis A and B and pertussis. Infants who are close contacts to the transplant recipient may be vaccinated against rotavirus (live vaccine).

Background

Vaccinations against a variety of bacterial or viral pathogens are an effective manner of preventing infection. Typically vaccinations begin in childhood and continue into early adulthood. A smaller number of vaccinations (i.e. yearly influenza, tetanus/diphtheria booster, pneumococcal vaccines) continue into adulthood.

Hematopoietic stem cell transplantation is an effective and well-accepted treatment for a variety of benign and malignant blood disorders as well as immune-based illnesses. Following hematopoietic transplantation, prior immunity is lost and must be regenerated. Consensus guidelines from all hematopoietic transplantation societies and infectious disease societies recommend revaccination as part of standard post-transplant supportive care to assist in recapitulation of immunity.

In Ontario, publicly funded vaccines and their schedules can be found at http://www.health.gov.on.ca/en/pro/programs/immunization/docs/immunization_schedule.pdf. Part 3 of the Canadian Immunization Guide outlines the recommendations for the immunocompromised population which includes those who have undergone a hematopoietic stem cell transplant (https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html). Other sources of information include the Centre for Disease Control (https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html). Many national and international transplant groups have also generated their own immunization recommendations.

This Position Statement outlines the consensus for vaccination for recipients of either an autologous or allogeneic hematopoietic stem cell transplant. The purpose of this document is to standardize the vaccination schedule for Ontario transplant patients. This information will be useful for stem cell transplant centres, and physicians caring for patients after transplant. This will also assist in identifying potential gaps in immunization funding.

Vaccinations of Close Contacts

Household and close contacts of stem cell transplant patients, including healthcare workers involved in the care of stem cell transplant patients, should have their immunizations up to date. Specifically, non-immune (either from lack of previous immunization or infection) close contacts should be immunized for MMR, varicella or zoster, influenza and hepatitis A and B. Close contacts should not be vaccinated with the Flumist® influenza vaccine since it contains live attenuated influenza virus and could pose a risk of transmitting influenza virus to the transplant recipient. Infants in close contact with transplant recipients may receive rotavirus vaccine. Specifics regarding the timing of vaccination and the potential for viral shedding and risk to the transplant recipient should be reviewed by the transplant team. Viral shedding may occur for potentially up to 6 weeks after the administration of live virus vaccine to any individual. This may require quarantine/isolation of the immune-suppressed patient, measuring whether there is residual IgG immunity to MMR/Varicella and/or treating patient with acyclovir.

Vaccinations Post-Transplant

In general, inactivated vaccines may be administered starting at least 3 months post-transplant, while select live vaccines (see details following) are introduced later, often at least 24 months post-transplant, provided that:

- patients are not still significantly immunosuppressed;
- patients are not experiencing graft versus host disease (GVHD);
- patients are not on corticosteroids or other immunosuppressants for at least 3 months, and
- the primary disease has not rendered the patient significantly immunosuppressed in an ongoing manner.

The transplant recipient's medical team would determine whether the patient has ongoing significant immunosuppression that may render live vaccine administration risky.

The latest version of the Public Health Agency of Canada's (PHAC) Immunization guide outlines the recommendations for the hematopoietic stem cell transplant population. Recommendations can be found at https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#p3c7t3.

A summary of the use of live and inactivated vaccines follow.

Live Vaccines

There are certain live vaccines that are considered contraindicated and should not be used in the hematopoietic stem cell transplant patient. These include BCG, live intranasal influenza vaccine, rotavirus, smallpox, live (oral) typhoid, and oral polio. Herpes zoster vaccine (Zostavax®), which is also live, should not be administered to stem cell transplant recipients either. It is felt that the increased number of viral units, approximately 15-fold, in the zoster vaccine (Zostavax®) as compared with varicella vaccine (Varivax®) may render it risky in transplant recipients. (see Inactivated Vaccines section below regarding Shingrix ®)

Other live vaccines may be used beginning at least 24 months after transplant, provided that the recipient does not have ongoing significant immunosuppression or chronic GVHD. Such vaccines include varicella, yellow fever and MMR. Varicella and MMR serological testing is available.

One approach used by the Fred Hutchinson Cancer Research Centre is to not give varicella or MMR vaccines unless the patient is at least 2 years post-transplant, at least 1 year off immuno-suppressive therapy, and at least 5 months since the last infusion of IVIG, plasma or VZIG (the 2-1-5 rule). For varicella in patients who are seronegative, one dose can be given with post varicella serology in case another dose is needed (after 1 month). It is prudent to ensure that there is seroconversion after a second dose of varicella vaccine, if needed. For MMR, perform IgG immunity test and if patient is lacking immunity to any component of MMR, administer one dose at least 24 months post-transplant with potentially another dose after at least 3 months if there is no seroconversion. The use of some live vaccines require expert consultation. For

example, yellow fever vaccine may only be required if traveling to an endemic area. Referral to specialized Travel Medicine/Infectious Disease clinics for comprehensive vaccine and disease prevention advice is encouraged for those who are planning to travel to 'exotic' areas.

Inactivated Vaccines

The following vaccines may be administered only if indicated, and are not needed routinely post-transplant: hepatitis A, cholera/traveler's diarrhea (inactivated oral), Japanese encephalitis, rabies, typhoid (inactivated intramuscular), tick-borne encephalitis, and HPV. Again, consultation with infectious disease specialists may be required for individual patients.

Regarding hepatitis A, if there is risk or travel, then 2 doses can be given each at least one month apart starting 6 to 12 months post-transplant. For Hepatitis B, the higher dose (40 ug/dose) vaccine is recommended over Twinrix® (which contains lower HBV antigen), so the stand-alone Hepatitis A (Havrix®) and B vaccines (Recombivax® or Engerix®) should be administered in the transplant population. Hepatitis B vaccine would be given at 3 doses starting 6 months post-transplant (see Table 1). Hepatitis serology can be used to confirm maintenance of immunity.

Regarding the HPV vaccine (Gardasil®) there is controversy. The CDC recommends HPV vaccination (3 doses) up to the age of 26 in females and males who have undergone a stem cell transplant. Other groups consider this vaccine optional given the lack of data and the fact that there are screening procedures in place for early detection of cervical cancer and pre-cancerous lesions. Based on PHAC, we recommend 3-dose HPV vaccine (at 6, 8 and 12 months post-transplant) for both females and males 9-26 years of age, and older depending on risk, in addition to ongoing cervical screening.

The use of live-attenuated vaccine for herpes zoster poses a risk in immunocompromised patients so the new Shingrix ® may be of benefit. Although the data are limited on the efficacy and safety of the Shingrix vaccine in the post-allogeneic HSCT population, Stadtmauer (Stadtmauer, 2014) concluded that the vaccine was well tolerated and immunogenic, with clinically acceptable safety profiles.

The following vaccines, based on the PHAC, are recommended post-transplant: diphtheria, pertussis, polio, tetanus, hepatitis B, influenza (inactivated), pneumococcal C-13 and P-23, hemophilus influenzae and meningococcal conjugate (quadrivalent). The following tables outline the vaccines and administration details.

Table 1. Suggested Vaccine Dosing Schedule

For the most recent information on scheduling, please refer to Public Health's Canadian Immunization Guide: Immunization of immunocompromised persons (https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a17).

Vaccine	When to Start	Dosing Schedule
Diphtheria*	6-12 months	3 doses, each one month apart§
Pertussis*	6-12 months	1 dose, if given alone (*see below*) §
Polio*	6-12 months	3 doses, each one month apart§
Tetanus*	6-12 months	3 doses, each one month apart§
Hepatitis B	6-12 months	3 doses, at 0, 1 and 6 months, use high dose vaccine (40ug dose), monitor HBsAb titres
Influenza (inactivated)	4-6 months	Annually
Pneumococcal C-13 (Prevnar®)	3-9 months	3 doses, 1 month apart
Pneumococcal P-23 (Pneumovax®)	6-12 months after last C-13 dose	1 dose with booster after 12 months
Hemophilus influenza*	6-12 months	3 doses, at least 4 weeks apart
Meningococcal Conjugate (quadrivalent)	6 months	1 dose. A second dose is only required if the first dose is given within 6 months of transplant (if so, the second dose can be given 2 months after the first dose).

Table 2: Sample Vaccination Schedule Template

Vaccine	Comments	Time Post-Transplant (months)							
		6	7	8	10	12	14	18	24
DTaP Hib IPV* (Pediacel®)	Diptheria, tetanus, pertussis, polio, Hemophilus influenzae b	x	x	x				x	
Hepatitis B (40 mcg)	High dose vaccine Monitor HBsAb titres yearly	x	x			x			
Hepatitis A (Havrix®)	If risks or travel present	x				x			
Pneumococcal C-13 (Prevnar®)		x	x	x					
Pneumococcal P-23 (Pneumovax®)^							x		
Meningococcal Conjugate (quadrivalent-Menactra®)		x		x					
Influenza		Yearly							
Varicella**	Additional dose 3 months later if no seroconversion								x
MMR**									x
HPV	Females and males 9-26 years of age, and older depending on risk	x		x		x			
Shingrix	Two doses at least 1 month apart								

*The DTaP-Hib-IPV vaccine includes diphtheria, tetanus, acellular pertussis, hemophilus influenza B and inactivated polio virus vaccine. Some jurisdictions administer this vaccine at 6, 7, 8 and 18 months post-transplant. In Canada the combination options are to give Pediacel® or Quadricel® with Act HIB vaccine.

^Followed by a booster dose 1 year after the initial dose

§Followed by a booster dose at 18 months

**check serology at 24 months prior to vaccination to optimize which patients may not need re-vaccination, particularly in autologous transplantation

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