Hematopoietic Stem Cell Transplantation (HSCT)

Hematopoietic stem cell transplantation (HSCT) results in immunosuppression from:

- Hematopoietic ablative therapy preceding transplant
- Medications used to prevent or treat graft-versus-host disease (GVHD)
- In some cases, the disease process necessitating the transplantation.

HSCT generally involves the ablation of the bone marrow followed by re-implantation of the person's own stem cells (autologous HSCT) or stem cells from a donor (allogeneic HSCT). Recipients of allogeneic grafts from donors who are not closely matched siblings are at substantially greater risk for GVHD, suboptimal graft function, and delayed capability for immune system memory.

Depending on the pre-ablation immune status of the client in autologous HSCT or on the immune status of the donor in allogeneic HSCT, there may be some immunity to vaccine preventable diseases following transplantation. However, antibody levels to vaccine preventable diseases decline 1-4 years after HSCT if the recipient is not re-immunized, regardless of whether the transplant was autologous or allogeneic. [A] As such, pre-vaccination serology is not recommended for HSCT recipients prior to vaccination. If an individual has been tested prior to vaccination and has evidence of immunity for a respective disease, they should be vaccinated regardless of these results.

HSCT recipients are at significant risk of developing life-threatening invasive pneumococcal disease (IPD). IPD rates in this group are between 1-10% with a median onset of 1 year following transplant. Because of the poor response to the pneumococcal polysaccharide vaccine in these recipients, individuals of all ages are recommended to receive the pneumococcal conjugate vaccine as well as the polysaccharide. [B] HSCT recipients are also recommended to receive higher potency DTaP products (i.e., the formulation used in young children in the routine immunization schedule) regardless of age. [B]

For scheduling guidance and as a paper record of immunizations, use Table 1: Worksheet for Immunization of Adult Hematopoietic Stem Cell Transplant (HSCT) Recipients (those 18 years of age and older) and Table 2: Worksheet for Immunization of Pediatric Allogeneic Hematopoietic Stem Cell Transplant (HSCT) Recipients (those under 18 years of age).

Most inactivated vaccines should be initiated **6-12** months post-HSCT. Patients receiving B-cell depleting agents (e.g., rituximab) should wait until 6 months after their last dose prior to initiation. However, inactivated influenza vaccine can be given as early as 4 months post-HSCT to provide protection during the influenza season (typically November – April). If given earlier than 6 months post-HSCT, a 2nd dose of inactivated influenza vaccine should also be given 4 weeks later. The HSCT specialist will determine the appropriate time to commence immunizations and will provide written guidance to the client for sharing with the immunizing Public Health Nurse.

Do not administer live vaccines until 24 months post-HSCT and then only if there is no ongoing anticancer therapy, immunosuppression, IVIg or subcutaneous Ig, or active graft-versus-host disease (GVHD). **Note**: BCG vaccine is contraindicated at all times.

[A] Advisory Committee on Immunization Practices. General Recommendations on Immunization. MMWR Recomm Rep. 2011;60(RR-2):1-60.

[B] Hilgendorf, et al. Vaccination of Allogeneic Haematopoietic Stem Cell Transplant Recipients: Report from the International Consensus Conference on Clinical Practice in Chronic GVHD. Vaccine. 2011 Apr;29(16):2825-33.

Inactivated zoster vaccine (SHINGRIX®) is recommended by the National Advisory Committee on Immunization (NACI) for those 50 years of age and older, and may be considered for immunocompromised individuals. Although this vaccine is not provided free in BC, it may be purchased without a prescription at most pharmacies and travel clinics. Live zoster vaccine is not recommended for HSCT recipients. For more information, see Part 4 – Biological Products, Zoster Vaccine (Recombinant): SHINGRIX®.

Table 1: Worksheet for Immunization of Adult Hematopoietic Stem Cell Transplant (HSCT) Recipients (those 18 years of age and older)

Date:	YYYY/MM/DD	Date of Transplant:	YYYY/MM/DD
CLIENT INFORMATION			
Name:	Last	First	
DOB:	YYYY/MM/DD	PHN:	

1st Visit (6-12 months after HSCT) [A]	2nd Visit (1 month after 1st visit)	3rd Visit (2 months after 1st visit)	4th Visit (8 months after 1st visit)	5th Visit (12 months after 1st visit)	6th Visit (> 24 months after HSCT)
Date given:	Date given:	Date given:	Date given:	Date given:	Date given:
DTaP-IPV-Hib [B]	DTaP-IPV-Hib [B]	DTaP-IPV-Hib [B]		DTaP-IPV-Hib [B]	
Hepatitis B [C, D]	Hepatitis B [C, D]	Hepatitis B [C, D]		Hepatitis B [C, D, E]	
	Hepatitis A			Hepatitis A [E]	
PCV13 [F]	PCV13 [F]	PCV13 [F]	PPV23 [F]		
Men-C-A,C,Y,W-135 [G]			Men-C-A,C,Y,W-135 [G]		
Influenza [H]					
		HPV [I]	HPV [I]		HPV [I]
					MMR [J, K]
					Varicella [K, L]

After each set of vaccines, a record of immunizations should be sent by fax to the attention of the Long Term Follow Up Clinic at the Leukemia/Bone Marrow Transplant Survivorship Program at Vancouver General Hospital, fax: (604) 875-4026.

A The HSCT specialist will determine the appropriate time to commence immunizations and will provide written guidance to the client for sharing with the Public Health Nurse.

B Use of pediatric formulation DTaP-IPV-Hib in this population is based on expert opinion from the adult HSCT program.

C Requires the higher vaccine dosing indicated in the Hepatitis B Vaccine Higher Dose Schedule. For programmatic reasons, HSCT recipients should follow the hepatitis B vaccine schedule indicated in the table above, using the age-appropriate higher vaccine dosing. The schedule in the table above is applicable to a 4-dose ENGERIX®-B series; for those using a RECOMBIVAX HB® or RECOMBIVAX HB® Dialysis (40 mcg/mL) product, a 3-dose schedule is required and the dose indicated at the 2nd visit can be eliminated. Note: If any dose in the series is given as ENGERIX®-B, a 4-dose series is recommended. For those 18 and 19 years of age, if RECOMBIVAX HB® (10 mcg/mL) adult presentation is unavailable, 2 vials of RECOMBIVAX HB® (5 mcg/0.5 mL) pediatric presentation may be used to administer a 1 mL (10 mcg) dose.

D Measure anti-HBs 1 month after vaccine series completion. If anti-HBs is < 10 IU/L, provide a second series of hepatitis B vaccine, using the Hepatitis B Vaccine Higher Dose Schedule. Retest anti-HBs 1 month after completion of the second series. If anti-HBs remains < 10 IU/L, consider as a non-responder and susceptible to hepatitis B. There is no benefit to further vaccination. If an exposure to blood or body fluids occurs, the client will require post-exposure prophylaxis.

E For programmatic reasons, the 4th dose of hepatitis B and the 2nd dose of hepatitis A are to be given at 18 months after HSCT. However, if the client presents earlier for the 4th dose of hepatitis B and the 2nd dose of hepatitis A, these vaccines can be administered following the recommended intervals, see Part 4 - Biological Products.

F **PCV13 is to be given using a minimum interval of 4 weeks between the 1st and 2nd dose and the 2nd and 3rd dose**. Administer PPV23 no earlier than 6 months after PCV13. A 2nd dose of PPV23 is recommended 5 years after the 1st dose of PPV23.

G A booster dose of Men-C-A, C, Y, W-135 conjugate vaccine is recommended every 5 years. See Part 4 - Biological Products, Meningococcal Quadrivalent Conjugate Vaccines.

H During influenza season (usually November to April) vaccination with influenza vaccine may commence 4 months after HSCT. If this is done < 6 months post-transplant, a 2nd dose should be offered 28 days later. Live attenuated influenza vaccine is contraindicated for HSCT clients.

I Eligible individuals (see Part 4 – Biological Products, Gardasil®9 for eligibility indications) should be offered a 3-dose vaccine series. Based on a risk assessment, HPV vaccination can be initiated as early as 6-12 months post-HSCT using a 0, 2, and 6 months schedule.

J Vaccination with MMR vaccine may be considered 24 months after transplantation provided there is no evidence of active graft-versus-host disease (GVHD), immunosuppression and anticancer therapy has been discontinued for at least 3 months (6 months for patients who have received B-cell depleting monoclonal antibodies, e.g., rituximab), IVIg or subcutaneous Ig has been discontinued for 8 months, and the person is deemed immunocompetent by a transplant specialist (**written approval required**). Provide 2 doses separated by 2 months and measure measles and rubella IgG 1 month after the 2nd dose. (NB: the serological correlates of protection for mumps have not been established).

K MMR and varicella vaccines may be given at the same time. If not given concomitantly, a minimum interval of 4 weeks is recommended between administration of the vaccines. See Immunization with Inactivated and Live Vaccines. MMRV is contraindicated.

L Varicella vaccination may be considered 24 months after transplantation provided there is no evidence of active graft-versus-host disease (GVHD), immunosuppression and anticancer therapy has been discontinued for at least 3 months (6 months for patients who have received B-cell depleting monoclonal antibodies, e.g., rituximab), IVIg or subcutaneous Ig has been discontinued for 8 months, and the person is deemed immunocompetent by a transplant specialist (**written approval required**). Provide 2 doses separated by 2 months, and measure varicella IgG 1 month after the 2nd dose, specifying on the Public Health Laboratory Serology Screening Requisition that the client is immunocompromised. If antibody is not detectable, the client should be offered varicella zoster immune globulin on subsequent exposure to wild-type varicella.

Table 2: Worksheet for Immunization of Pediatric Allogeneic Hematopoietic Stem Cell Transplant (HSCT) Recipients (those under 18 years of age)

Date:	YYYY/MM/DD	Date of Transplant:	YYYY/MM/DD
CLIENT INFORMATION			
Name:	Last	First	
DOB:	YYYY/MM/DD	PHN:	

1st Visit (6-12 months after HSCT) [A]	2nd Visit (1 month after 1st visit)	3rd Visit (2 months after 1st visit)	4th Visit (8 months after 1st visit)	5th Visit (24 months after HSCT)	6th Visit (> 30 months after HSCT)
Date given:	Date given:	Date given:	Date given:	Date given:	Date given:
DTaP-IPV-Hib [B]	DTaP-IPV-Hib [B]	DTaP-IPV-Hib [B]		DTaP-IPV-Hib [B]	
	Hepatitis A [C]		Hepatitis A		
Hepatitis B [D]	Hepatitis B [D]		Hepatitis B [D]		
PCV13	PCV13	PCV13		PCV13	PPV23 [E]
Men-C-A,C,Y,W-135 [F]		Men-C-A,C,Y,W-135 [F]			
Inactivated Influenza [G]					
		HPV [H]	HPV [H]		HPV [H]
				MMR [I, J]	
				Varicella [I, K]	

A The HSCT specialist will determine the appropriate time to commence immunizations and will provide written guidance to the client for sharing with the Public Health Nurse.

B DTaP-IPV-Hib: In pediatric allogeneic HSCT patients, the Hepatitis B Vaccine Higher Dose Schedule is required. INFANRIX hexa® should not be used due to potency of the hepatitis B component. The use of pediatric formulation combination vaccines (higher potency vaccines) in those older than 7 years is based on expert opinion (Hilgendorf et al. Vaccination of Allogeneic Haematopoietic Stem Cell Transplant Recipients: Report from the International Consensus Conference on Clinical Practice in Chronic GVHD. Vaccine 2011 Apr;29(16):2825-33).

C Hepatitis A: The risk of hepatitis A acquisition should be assessed at the first visit. If travel outside of the country is planned, or if the child is of aboriginal ancestry or has other risk factors for hepatitis A acquisition this vaccine should be offered at the first visit.

D Hepatitis B: Use monovalent vaccine. Requires the higher vaccine dosing indicated in the Hepatitis B Vaccine Higher Dose Schedule. For programmatic reasons, HSCT recipients should follow the hepatitis B vaccine schedule indicated in the table above, using the age-appropriate higher vaccine dosing. NOTE: In order to reduce the total volume of vaccines at each visit, if RECOMBIVAX HB® (10 mcg/mL) adult presentation is unavailable, 2 vials of RECOMBIVAX HB® (5 mcg/0.5 mL) pediatric presentation may be used to administer a 1 mL (10 mcg) dose. For those 16 years of age and older, if **any** dose in the series is given as ENGERIX®-B, a 4-dose series is required at 0, 1, 2 and 6 months; a maximum volume of 2 mL for the deltoid sites may be considered for those with adequate muscle mass (Alberta Health Services, Standard for the Administration of Vaccines, 2018). One month after vaccine series completion, perform serology for anti-HBs. If testing indicates inadequate protection, provide a 2nd series, using the Hepatitis B Vaccine Higher Dose Schedule. Retest anti-HBs 1 month after completion of the 2nd series. If anti-HBs remains < 10 IU/L, consider as a non-responder and susceptible to hepatitis B. There is no benefit to further vaccination. If an exposure to blood or body fluids occurs, the client will require post-exposure prophylaxis.

E PPV23: Administer PPV23 at least 6 months after the last dose of PCV13 and/or when recipient reaches 2 years of age. Give a 2nd dose of PPV23 1 year after the 1st dose.

F Men-C-A,C,Y,W-135: See Part 4 - Biological Products, Meningococcal Quadrivalent Conjugate Vaccines, for vaccine specific information. A booster dose is recommended every 5 years.

G Inactivated Influenza: Inactivated influenza vaccine may be given as early as 4 months post-HSCT. If it is given before 6 months post-HSCT, 2 doses should be given 28 days apart regardless of history of influenza vaccine. Live attenuated influenza vaccine is contraindicated in HSCT patients.

H HPV: HPV vaccine should be offered to eligible HSCT recipients at 10 years of age and older. A 3-dose schedule should always be used. Based on a risk assessment, HPV vaccination can be initiated as early as 6-12 months post-HSCT using a 0, 2, and 6 months schedule.

I MMR and Varicella: Vaccination may be considered 24 months after transplantation provided there is no evidence of active graft-versus-host disease (GVHD), immunosuppression and anticancer therapy has been discontinued for at least 3 months (6 months for patients who have received B-cell depleting monoclonal antibodies, e.g., rituximab), IVIg or subcutaneous Ig has been discontinued for 8 months, and the person is deemed immunocompetent by a transplant specialist (**written approval required**). Refer to Immunization with Inactivated and Live Vaccines. In this population, MMR and varicella should NOT be given on the same day and should be separated by 4 weeks; MMRV is contraindicated.

J MMR: Provide 2 doses separated by 2 months, and measure measles and rubella IgG 1 month after the 2nd dose. (NB: The serological correlates of protection for mumps have not been established).

K Varicella: Provide 2 doses separated by 3 months, and measure varicella IgG 1 month after the 2nd dose, specifying on the Public Health Laboratory Serology Screening Requisition that the client is immunocompromised. If antibody is not detectable, the client should be offered varicella zoster immune globulin on subsequent exposure to wild-type varicella.

References

Hilgendorf I, Freund M, Jilg W, Einsele H, Gea-Banaloche J, Greinix H, et al. Vaccination of allogeneic haematopoietic stem cell transplant recipients: Report from the International Consensus Conference on Clinical Practice in chronic GVHD. Vaccine 2011 Apr;29(16):2825-33.

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