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.

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. [A] HSCT recipients are also recommended to receive higher potency DTaP products regardless of age. [A]

Use Table 1: Worksheet for Immunization of Adult Hematopoietic Stem Cell Transplant (HSCT) Recipients (those 18 years of age and older) for scheduling guidance and as a paper record of immunizations.

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

Most inactivated vaccines should be initiated **6-12** months post-HSCT. Inactivated influenza vaccine can be given at 6 months post-HSCT or as early as 4 months. If given before 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 Public Health Nurse.

Do not administer live vaccines until 24 months post-HSCT and then only if there is no ongoing immune suppressive treatment or graft-versus-host disease (GVHD).

Note: BCG is contraindicated at all times. Live zoster vaccine is not recommended.

[A] 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.

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, 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. In order to reduce the total volume of vaccines at each visit, for those 20 years of age and older, RECOMBIVAX HB® Dialysis formulation (40 mcg/mL) may be used. 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. Note: If the series is initiated with ENGERIX®-B, a 4-dose series at 0, 1, 2, 6 months is recommended.

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 3rd 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 3rd 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 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 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 graft-versus-host disease (GVHD), immunosuppression has been discontinued for at least 3 months, and the person is deemed immunocompetent by a transplant specialist (**written approval required**). Measure serology 1 month after MMR vaccination. If titers are not protective for measles or rubella give a 2nd dose of MMR **3 months after the 1st 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.

L Check serologic status (test for varicella IgG using the Public Health Laboratory Serology Screening Requisition and specify that the client is immunocompromised) prior to vaccination and administer vaccine to serologically varicella susceptible persons only. Varicella vaccination may be considered 2 years after transplantation provided there is no evidence of GVHD, immunosuppression has been discontinued for at least 3 months, and the person is deemed immunocompetent by a transplant specialist (**written approval required**). **Give only 1 dose**. One month after varicella vaccine, test for varicella IgG and specify 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.

Adapted from:

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;29(16):2825-33.

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

Advisory Committee on Immunization Practices. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions. MMWR Recomm Rep. 2012;61(40):816-819.

National Advisory Committee on Immunization. Update on the invasive meningococcal disease and meningococcal vaccine conjugate recommendations. Can Comm Dis Rep.2009;36(ACS-3):1-40.

Canadian Immunization Guide. Part 4, Active Vaccines (Chapters on Measles and Varicella Vaccines).

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]					
				MMR [H, I]	
				Varicella [H, J]	
		HPV [K]	HPV [K]		HPV [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. NOTE: If the series is initiated with ENGERIX®-B, a 4-dose series at 0, 1, 2, 6 months is recommended. 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 MMR and Varicella: Wait at least 24 months after ablative therapy before administering live vaccines and then only if immunosuppressive treatment has been discontinued for at least 3 months and there is no ongoing graft-versus-host disease (GVHD). Only give MMR and varicella vaccines with **written approval** from the most appropriate physician or nurse practitioner. 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.

I MMR: Measure the recipient's serology 4 weeks after the 1st dose of MMR. If non-immune to measles or rubella, give a 2nd dose of MMR 3 months after the 1st dose. (NB: The serological correlates of protection for mumps have not been established).

J Varicella: HSCT recipients should not receive more than 1 dose of varicella vaccine (Canadian Immunization Guide). One month after receipt of the vaccine, test for varicella IgG using the Public Health Laboratory Serology Screening Requisition and specify 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.

K 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.