Immunization in Paediatric Solid Organ Transplantation in Canada: A consensus statement from the Paediatric Group of the Canadian Society of Transplantation

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Introduction

Paediatric solid organ transplant recipients are at increased risk of severe illnesses from many vaccine-preventable diseases. Adequate immunization prior to solid organ transplantation can help reduce the risk of serious illnesses and/or death and impact outcomes in the paediatric transplant recipient. Ideally, children should complete age-appropriate immunizations before solid organ transplantation, and as early in the course of disease as possible to maximize the chance of immunological response. Where appropriate, accelerated immunization schedules may be possible for some vaccines to facilitate optimal dosing and response without unacceptable delay of the transplantation. Antibody response can be confirmed for certain vaccines where serologic assays are available.

This Canadian Society of Transplantation (CST) Paediatric Group consensus statement on recommended immunization pre- and post-transplantation aims to ensure that all paediatric solid organ transplant recipients have access to the same National Standard of Care across Canada. These recommendations are based on the Canadian Immunization Guideline,[1] the American Society of Transplantation (AST) recommendations,[2] the Centre for Disease Control (CDC) Advisory Committee on Immunization Practices (ACIP),[3] the Infectious Diseases Society of America recommendations,[4] The Canadian Paediatric Society, The Hospital for Sick Children, Toronto's Pre- and Post-transplant Immunization Guidelines (Solid Organ Transplant, Dec 2017),[5] clinical consensus guidelines on live-attenuated vaccines post-transplantation (published September 2019)[6] and clinical experts across Canada.

Since the availability of public funding for vaccination and vaccine products might differ in each province, each center should consult with local Infectious Disease (ID) specialist, paediatric solid organ transplant physicians and/or pharmacists as appropriate for province- and patient-specific issues.

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Inactive Vaccines

- Routine vaccines should be administered PRE-transplant when possible
- Delay transplantation for 2 weeks (if possible) following administration of inactive vaccines to ensure adequate vaccine response
- Accelerated regimen schedules may be possible for certain vaccines – please refer to tables for minimum age and interval recommended for accelerated scheduling
- For province-specific information about routine number of doses required and schedule details, please refer to local/provincial routine immunization schedule
- Routine vaccines should be restarted around 6 months post-transplant and/or once on baseline/low level immunosuppression to ensure optimal response, *except*:
    - Influenza seasonal vaccine (inactivated) may be administered as early as 1 month post-transplant
- Siblings and family members should be vaccinated as per routine guidelines

Table 1: Inactive vaccines (Diphtheria, Pertussis, Tetanus, Polio, Haemophilus Influenza B, Meningococcal, Pneumococcal, Hepatitis A, Hepatitis B, Human papillomavirus, Influenza)

Vaccine	Minimum age for 1st dose	Minimum interval between doses	Pre-transplant	Post-transplant and/or booster	Serology testing pre/post-vaccine
Diphtheria, pertussis, tetanus, polio, H. influenza B (DTaP-IPV-Hib)	6 weeks[7]	<u>Doses 1, 2, 3:</u> Min 4 weeks <u>Doses 3 to 4:</u> Min 6 months but must be repeated after 12 months[1, 3, 4, 8, 9]	Yes	Yes <u>If not vaccinated/ incomplete series:</u> • Start 1 year post-transplant • May start as early as 4 months in special circumstances (consult ID) <u>If vaccinated pre-transplant:</u> • Hib x1 (1 year post-transplant if more >5 years of age)[1] *Alternatively as booster[5]: • DTaP-IPV-Hib x1 (1 year post-transplant) • DTaP-IPV x1 (4-5 years post-transplant) Td booster every 10 years	Not routine
Polio, H.influenza B (IPV/Hib)					
Diphtheria, pertussis, tetanus, polio (DTaP-IPV)					

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Vaccine	Minimum age for 1st dose	Minimum interval between doses	Pre-transplant	Post-transplant and/or booster	Serology testing pre/post-vaccine
Tetanus (Td) Diphtheria, pertussis, tetanus (Tdap)	7 years[7]	<u>Doses 1, 2:</u> Min 2 months <u>Dose 3:</u> Min 6-12 months after *typically 1 dose unless used as primary series	Yes	Yes <u>If not vaccinated/ incomplete series:</u> • Start 1 year post-transplant • May start as early as 4 months in special circumstances (consult ID) <u>If vaccinated pre-transplant:</u> • Hib x1 (1 year post-transplant if more >5 years of age)[1] *Alternatively as booster[5]: • DTaP-IPV-Hib x1 (1 year post-transplant) • DTaP-IPV x1 (4-5 years post-transplant) Td booster every 10 years	Not routine
Meningococcal C (Men-C-C)	2 months	Menjugate: 1 month[10] NeisVac-C: 2 months[11]	Yes *transplant candidates are considered high risk due to impending immunosuppression	Yes <u>If not vaccinated/ incomplete series:</u> • Start as early as 6 months post-transplant <u>If vaccinated pre-transplant:</u> • Men-C-ACWY x1 (≥2 months of age)[12] (give at 6-12 months post-transplant)	Not routine
Meningococcal quadrivalent (Men-C-ACWY)	Menactra: 9 months[3, 8, 13] Menveo: 2 months[3, 14] Nimenrix: 6 weeks[15]	1-3 doses (vaccine specific) Menactra: 3 months Menveo and Nimenrix: 2 months			Not routine

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Vaccine	Minimum age for 1st dose	Minimum interval between doses	Pre-transplant	Post-transplant and/or booster	Serology testing pre/post-vaccine
Serogroup B Meningococcal (4CMenB)	2 months	3 dose schedule: 1 month[16] 2 dose schedule: 2 months[16]	Yes *transplant candidates are considered high risk due to impending immunosuppression	Yes *transplant recipients are considered high risk due to concurrent immunosuppression	Not routine
Pneumococcal conjugate vaccine (PCV13)	6 weeks	8 weeks[1, 7] *4-8 weeks[17]	Yes	Yes <u>If not vaccinated/ incomplete series:</u> • Start as early as 6 months post-transplant <u>If vaccinated pre-transplant:</u> • PCV x1 (6-12 months post-transplant), then • PPV x1 (3-5 years post-transplant) *alternatively used for booster dosing[5]	Not routine
Pneumococcal polysaccharide (PPV)	2 years	2 doses for high-risk: Min 6-8 weeks post-conjugate vaccine			Not routine
Hepatitis A	6 months[1]	6 months[1]	Yes *NACI does not recommend Twinrix® or Twinrix® Junior in immunosuppressed or hyporesponsive (ie ESRD on dialysis)[1]	Yes <u>If not vaccinated/ incomplete series:</u> • Start as early as 6 months post-transplant <u>If vaccinated pre-transplant:</u> • Consider booster based on serology	Not routine May be considered in high risk patients who were immunized post-transplant

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Vaccine	Minimum age for 1st dose	Minimum interval between doses	Pre-transplant	Post-transplant and/or booster	Serology testing pre/post-vaccine
Hepatitis B	Newborn *6 months for combination Hep A-B[1] (Twinrix/ Twinrix Junior) *6 weeks for DTaP-HB-IPV-Hib (INFANRIX hexa)[18]	<u>Accelerated:</u> *4 doses*: 0, 7, 21-28 days and booster at 6-12 months *3 doses*: 0, 1, >2 months[7]	Yes *NACI does not recommend Twinrix® or Twinrix® Junior in immunosuppressed or hyporesponsive (ie ESRD on dialysis)[1]	Yes <u>If not vaccinated/ incomplete series:</u> • Start 1 year post-transplant • May start as early as 6 months post-transplant for high-risk (ie. Travel) <u>If vaccinated pre-transplant:</u> • Repeat series (3-4 doses) x1 if seronegative at 1 year post-transplant In post-transplant patients, double dose (in microgram) for age is recommended	Yes • 6-8 weeks post-series • Annually post-series • If seronegative, repeat series x1 • If non-responsive with repeat series, consider double-dose for age and consult ID
Human papilloma virus (HPV)	9 years[1, 7] *may be considered if ≥7 years if due for transplant	Doses 1 to 2: Min 4 weeks Doses 2 to 3: Min 12 weeks[1, 7] 3rd dose ≥24 weeks after 1st dose[1, 7]	Yes[2, 3, 8, 19] *Immunocompetent patients can be considered for 2-dose regime: min interval of 5 months between dose 1 and 2	Yes May be started as early as 3-6 months post-transplant	Not routine

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Vaccine	Minimum age for 1st dose	Minimum interval between doses	Pre-transplant	Post-transplant and/or booster	Serology testing pre/post-vaccine
Influenza (Trivalent and quadrivalent inactivated)	6 months[1]	Annual	Yes *quadrivalent vaccine preferred for paediatric patients	Yes May be started as early as 4 months post-transplant May consider as early as 1 month post-transplant if: • Influenza outbreak • Transplanted just prior to flu season If immunized at 1 month post-transplant, may consider 2nd dose at 3-4 months post-transplant if influenza outbreak still ongoing. Consult ID if influenza outbreak.	Not routine

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Live Vaccines

- Delay transplantation for 4 weeks following administration of live vaccines[4, 8]
- Live vaccines should be administered PRE-transplant when possible
- Accelerated regimen schedules may be possible for certain vaccines – please refer to tables for minimum age and interval recommended for accelerated scheduling
- For province-specific information about routine number of doses required and schedule details, please refer to local/provincial routine immunization schedule
- [¥]Live vaccines are CONTRAINDICATED POST-transplant based on *current* guidelines, however:
    - A new consensus guideline on live vaccinations post-transplantation was proposed by a panel of international experts (see table 3).[6]
    - The CST Paediatric group acknowledges that there is paucity of evidence of efficacy, safety and/or risks to inform recommendations for or against live vaccination in specific organ groups (refer to footnote[a] in Table 3). Therefore, for these organ groups, we are of the opinion that they can be evaluated for live vaccination post-transplantation "with caution" on a case-by-case basis, taking into consideration the patient's overall degree of immunosuppression, with the guidance of local paediatric transplant, infectious disease and immunology experts. If considered, these evaluations should occur within the context of locally approved guidelines and a quality improvement framework that includes risk assessment/stratification, informed consent and post-vaccine monitoring for adverse events.
    - We recommend that those in the "Vaccine with caution" group (Table 3 – Group 3) should also be considered for live vaccination within the context of locally approved guidelines and a quality improvement framework that includes risk assessment/stratification, informed consent and post-vaccine monitoring for adverse events.
- Siblings and family members should be vaccinated as per routine guidelines.
    - It is safe for siblings and family members of solid organ transplant recipients to receive live vaccines, except oral polio.

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Table 2: Live vaccines (Mumps, Measles, Rubella, Varicella, Rotavirus, Influenza)

Vaccine	Min age for 1st dose	Min interval between doses	Pre-transplant	Post-transplant and/or booster	Serology testing pre/post-vaccine
Mumps, Measles, Rubella (MMR)	6 months	4-6 weeks in consultation with ID[1, 2, 7, 8, 20, 21]	Yes	¥No	Not routine
Mumps, Measles, Rubella, Varicella (MMR-V)	Priorix-Tetra: 9 months ProQuad: 12 months	Min 4 weeks in consultation with ID[3, 7, 22, 23]	Yes	¥No	Not routine
Varicella	12 months *Alternatively used in accelerated schedule: 6 months[24]	Varivax III: 4 weeks[2, 3, 8, 22, 25] Varilrix: 6 weeks[23]	Yes	¥No	Yes. Check serology 4-6 weeks post-last dose
Rotavirus	6 weeks[1] Max: <15 weeks	4 weeks[1]	Yes	No	Not routine
Influenza (intranasal, live-attenuated)	2 years[26]	Annual	Yes	No	Not routine

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Table 3: Live vaccination after paediatric solid organ transplant: Recommendations from international expert consensus meeting in 2018[6]
*taken from Table 2 in the consensus guideline publication by Suresh et.al. Pediatr Transplant 2019

Groups	Recommendations	Criteria

Group 1: Defer vaccine	Live vaccine post-solid organ transplant should be deferred	• Clinically unwell
		• Cardiac, lung and multi-visceral transplant[a]
		• High-level immunosuppression
		• Patients with current rejection
		• Use of novel biologic agents (other than those outlined in table)
		• Use of following agents:
		  • Anti-thymocyte globulin <1 year prior
		  • Alemtuzumab <2 years prior
		  • Rituximab <1 year prior

Group 2: Proceed with vaccine	Live vaccine post-solid organ transplant is considered to be likely safe	• Clinically well
		• Do not meet criteria in Group 1 or 3 and meets all 3 of following criteria:
		1. Timeline criteria:
		  • 1 year post-transplant AND
		  • 2 months post-rejection episode
		AND
		2. Intensity of immunosuppression criteria:
		  • Steroids (prednisone equivalent) <2 mg/kg/day or total cumulative <20 mg/day
		  • Tacrolimus or sirolimus <8 ng/ml for 2 consecutive readings
		  • Cyclosporine <100 ng/ml for 2 consecutive readings
		AND
		3. Minimum immune criteria:
		  • ALC
		  • >1500 cells/ µL (children ≤6 years)
		  • >1000 cells/µL (children >6 years)
		  • CD4
		  • >700 cells/µL (children ≤6 years)
		  • >500 cells/µL (children >6 years)
		  • Normal total serum IgG for age

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Groups	Recommendations	Criteria

Group 3: Vaccine with caution	Live vaccine post-solid organ transplant may be considered after in-depth evaluation, provided minimum timeline, immunosuppression and immunology criteria in Group 1 are met	• Patients on mycophenolate mofetil (MMF)/ mycophenolate sodium
		• Patients who have received T cell depleting agents:
		  • Anti-thymocyte globulin – wait 1 year[b]
		  • Alemtuzumab – wait 2 years[b]
		• Patients who have received Rituximab – wait 1 year[b]
		• Patients with persistent elevation of EBV viral loads
		• Liver transplant recipients undergoing immunosuppression withdrawal with the goal of cessation or those deemed to have 'functional tolerance'

[a]Insufficient evidence to provide recommendations for live vaccination after heart, lung, intestine or multi-visceral transplant. Therefore, these transplant groups may be excluded based on their net state of immunosuppression or until further evidence is available

[b]Wait stated time interval prior to further evaluation and consideration for live vaccination

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Travel Vaccines

- Prior to travel, all transplant candidates and recipients should consult Infectious Diseases and/or Travel Clinic for recommended immunizations
- Patients and families need to plan consultation well ahead of time as some vaccines need to be administered several weeks prior to travel to ensure adequate protection
- Families should budget for the cost of consultation and vaccines as most travel clinic consultation and vaccines are not covered by provincial health plans

Table 4: Travel vaccines

Vaccine	Min age for 1st dose	Min interval prior to travel	Pre-transplant	Post-transplant	Serology testing pre/post-vaccine
Enterotoxigenic E. coli (inactivated)	2 years[27]	2 weeks[27]	Yes	Yes	Not routine
Hepatitis A	6 months[1]	2-4 weeks	Yes	Yes	Not routine
Hepatitis B	Newborn[1]	Accelerated: given Days 0, 7, 21 with booster at 6-12 months (upon return)	Yes	Yes In post-transplant patients, double dose (in microgram) for age is recommended	Yes • 6-8 weeks post-series • Annually post-series • If seronegative, repeat series x1 • If non-responsive with repeat series, consider double-dose for age and consult ID
Combination Hepatitis A-B	6 months[1]	Accelerated schedule as above with Twinrix	Yes *NACI does not recommend in immunosuppressed or hyporesponsive (ie ESRD on dialysis)[1]	No *NACI does not recommend in immunosuppressed[1]	

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Vaccine	Min age for 1st dose	Min interval prior to travel	Pre-transplant	Post-transplant	Serology testing pre/post-vaccine
Japanese encephalitis (inactivated)	2 months[8, 28]	Consult travel clinic	Yes	Yes	Not routine
Rabies (inactivated)	Newborn	7 days	Pre-exposure: No (unless immunocompromised and expecting intense animal exposure) Post-exposure: Yes	Yes <u>Pre-exposure vaccine:</u> • Can be started 6-12 months post-transplant for individuals expecting intense animal exposure or who will be distant from medical care <u>Post-exposure vaccine:</u> Recommended for any post-transplant patient	Pre-exposure: Not routine unless immunosuppressed Post-exposure: Consider serology 7-14 days post-completion. If titre <0.5, re-vaccinate with 2nd series
Salmonella Typhi (inactivated) IM	2 years[29]	14 days[1]	Yes	Yes Re-immunize every 2-3 years if at ongoing risk[1]	Not routine

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Vaccine	Min age for 1st dose	Min interval prior to travel	Pre-transplant	Post-transplant	Serology testing pre/post-vaccine
Salmonella Typhi (live-attenuated) Oral	5 years[30]	7 days	Yes	No	Not routine
Salmonella Typhi-Hep A (inactivated) IM	16 years[31]	14 days	Yes	Yes	Not routine
Yellow Fever (live-attenuated)	9 months[32]	10 days[32]	Yes	No	For immunocompromised: consider testing 2-5 years post-vaccine and/or post-transplant

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References:

1. National Advisory Committee on Immunization: Canadian Immunization Guide. 2018.
2. Danziger-Isakov, L, Kumar, D, Practice, ASTIDCo: Vaccination in solid organ transplantation. *Am J Transplant,* 13 Suppl 4**:** 311-317, 2013.
3. Advisory Committee on Immunization Practices: Recommended immunization schedule for children and adolescents aged 18 years or younger, United States 2018. 2018.
4. Rubin, LG, Levin, MJ, Ljungman, P, Davies, EG, Avery, R, Tomblyn, M, Bousvaros, A, Dhanireddy, S, Sung, L, Keyserling, H, Kang, I, America, IDSo: 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis,* 58**:** 309-318, 2014.
5. Immunization Working Group on behalf of the Transplant & Regenerative Medicine Centre Clinical Practice Committee, THfSC, Toronto,: Pre- and post-transplant immunization guidelines: Solid organ transplant. 2017.
6. Suresh, S, Upton, J, Green, M, Pham-Huy, A, Posfay-Barbe, KM, Michaels, MG, Top, KA, Avitzur, Y, Burton, C, Chong, PP, Danziger-Isakov, L, Dipchand, AI, Hebert, D, Kumar, D, Morris, SK, Nalli, N, Ng, VL, Nicholas, SK, Robinson, JL, Solomon, M, Tapiero, B, Verma, A, Walter, JE, Allen, UD: Live vaccines after pediatric solid organ transplant: Proceedings of a consensus meeting, 2018. *Pediatr Transplant,* 23**:** e13571, 2019.
7. Publicly funded immunization schedules for Ontario. 2016.
8. Abuali, MM, Arnon, R, Posada, R: An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. *Pediatr Transplant,* 15**:** 770-777, 2011.
9. Sanofi Pasteur: Product monograph-Pediacel. 2012.
10. Novartis: Product monograph-Menjugate. 2013.
11. Pfizer Canada Inc: Product monograph-NeisVac-C. 2019.
12. Robinson, JL: Update on invasive meningococcal vaccination for Canadian children and youth. *Paediatr Child Health,* 23**:** e1-e4, 2018.
13. Sanofi Pasteur: Product monograph-Menactra. 2017.
14. GlaxoSmithKline Inc: Product monograph-Menveo. 2019.
15. Pfizer Canada Inc: Product monograph-Nimenrix. 2018.
16. GlaxoSmithKline Inc: Product monograph-Bexsero. 2019.
17. T.M.Wyeth LLC, PCU: Product monograph-Prevnar 13. 2019.
18. GlaxoSmithKline Inc: Product monograph-Infanrix hexa. 2018.
19. Kumar, D: Immunizations following solid-organ transplantation. *Curr Opin Infect Dis,* 27**:** 329-335, 2014.
20. L'Huillier, AG, Kumar, D: Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Hum Vaccin Immunother,* 11**:** 2852-2863, 2015.
21. GlaxoSmithKline Inc: Product monograph-Priorix. 2019.
22. Merck Canada Inc: Product monograph-Varivax III. 2018.
23. GlaxoSmithKline Inc: Product monograph-Varilrix. 2019.
24. Alberta Government: Immunization for Children Expecting Solid Organ Transplant before 18 Months of Age (Accelerated). 2020.
25. Verolet, CM, Posfay-Barbe, KM: Live virus vaccines in transplantation: friend or foe? *Curr Infect Dis Rep,* 17**:** 472, 2015.
26. AstraZeneca Canada: Product monograph-Flumist Quadrivalent. 2018.

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27. Sanofi Pasteur: Product monograph-Dukoral. 2015.
28. Vanleva Austria GmbH: Product monograph-Ixiaro. 2018.
29. Sanofi Pasteur: Product monograph-Typhim Vi. 2018.
30. Pax Vax Berna GmbH: Product monograph-Vivotif. 2018.
31. Sanofi Pasteur: Product monograph-ViVAXIM. 2015.
32. Sanofi Pasteur: Product monograph-YF-Vax. 2019.

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