

Personalization of Immunization Recommendations for Immunocompromised Children

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Disclosures

- I have grant funding from the following agencies:
 - Public Health Agency of Canada
 - Canadian Institutes of Health Research
 - Canadian Donation and Transplantation Research Program
 - Canadian Immunity Task Force
- I will be discussing off label use of live attenuated varicella vaccines and live attenuated combined measles, mumps and rubella vaccines

Objectives

- Appreciate the general principles pertaining to immunizing immunocompromised children
- Describe research and clinical guidance supporting the use of live vaccines in select children who have had organ transplants
- Discuss the importance of individualizing vaccine recommendations for immunocompromised individuals

Immunization in Immunocompromised Populations – WHY?

- Considerable morbidity and mortality from common vaccine-preventable diseases

Statement from the Chief Public Health Officer of Canada on Global Increase in Measles and Risk to Canada

From: [Public Health Agency of Canada](#)

Statement

February 23, 2024 | Ottawa, ON | Public Health Agency of Canada

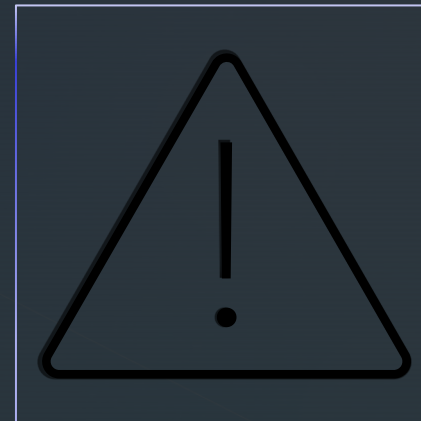
Principles of Immunization in Immunocompromised Hosts

Maximize benefit

- Vaccine choice
- Optimal timing
- Optimal dose
- Number of doses
- Dosing interval

Minimize harm

- Caution with live vaccines



Immunize when the best response is anticipated



Appropriate age



Early in disease course



Prior to Immunosuppression

Time of lowest
immunosuppression



Remote from administration of
blood products

Measles Mumps Rubella
and Varicella vaccines

Consider the individual's environment

- Encourage immunization of household members and close contacts

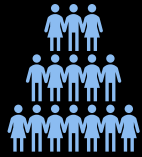




Caution with live vaccines

- Contraindicated for many immunocompromised individuals
- Administer at least 4 weeks prior to immunosuppression
- Can be safely used in select immunocompromised populations

Immunization in immunocompromised Individuals is complex!



We all have a role!



Open communication is Key!

patients/families, care teams, public health, vaccine providers



Engagement of other experts as required

Infectious Diseases
Immunology

Special Immunization Clinic (SIC) Network

- Assessment and management of patients with
 - challenging adverse events following immunization (AEFI)
 - medical conditions that may affect vaccine response or safety



Use of Live Varicella Vaccine in Pediatric Solid Organ Transplant (SOT) Recipients



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

American Journal of Transplantation

journal homepage: www.amjtransplant.org

Original Article

Safety and immunogenicity of the live-attenuated varicella vaccine in pediatric solid organ transplant recipients: A systematic review and meta-analysis

Received: 11 April 2019 | Revised: 12 July 2019 | Accepted: 26 July 2019

DOI: 10.1111/ptr.13571

ORIGINAL ARTICLE

WILEY

Live vaccines after pediatric solid organ transplant: Proceedings of a consensus meeting, 2018

Received: 7 March 2023 | Revised: 28 July 2023 | Accepted: 1 September 2023

DOI: 10.1111/ptr.14609

ORIGINAL ARTICLE

WILEY

Parent and healthcare provider views of live varicella vaccination of pediatric solid organ transplant recipients

JAMA Network | **Open**[™]

Original Investigation | Infectious Diseases

Safety and Immunogenicity of Live Viral Vaccines in a Multicenter Cohort of Pediatric Transplant Recipients

Piche-Renaud et al. Am J Transplant 2023
Suresh et al, Pediatr Transplant 2019
Condán et al. Pediatr Transplant 2023
Feldman et al. JAMA Netw Open 2023











Why?

- Risk of severe varicella disease
- Burden of post-exposure prophylaxis
- Immunization with varicella vaccine challenging pre-transplant
- Historically live attenuated varicella vaccine (LAVV) contraindicated after SOT

ORIGINAL ARTICLE

WILEY

Live vaccines after pediatric solid organ transplant: Proceedings of a consensus meeting, 2018

Sneha Suresh¹  | Julia Upton² | Michael Green³  | Anne Pham-Huy⁴ |
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Melinda Solomon¹⁸ | Bruce Tapiero¹⁹ | Anita Verma²⁰ | Jolan E. Walter^{21,22} |
Upton D. Allen²³ 

Data supports the safety and immunogenicity of LAVV in select pediatric SOT recipients

Most data in
liver and renal
recipients

Over 80%
seroconversion
to positive
varicella IgG

Suresh et al, *Pediatr Transplant*, 2019
Dipchand et al. *J Heart Lung Transplant* 2022
Verolet et al. *Transplantation* 2019
Gumm et al. *Pediatr Transplantation* 2021
Laue et al. *Children* 2022
Piché-Renaud et al. *Am J Transplant* 2023



Safety of LAAV after SOT

- Rash
 - Generally resolved without treatment
 - 13/635 suspected vaccine-strain varicella
 - Treated with antivirals, full recovery
- No signal for increased rejection

POST TRANSPLANT

DEFER

- Clinically unwell
- Current rejection
- High level immune suppression
- Recent or novel biologic use
- Underlying primary immunodeficiency
- Heart, Lung or Multivisceral transplant*

CAUTION

- MMF
- History of ATG/Alemtuzumab/Rituximab
- Persistently elevated EBV
- Functional Tolerance

VACCINATE

- Ensure all timeline, immunosuppression & immune criteria are met
- Obtain informed consent
- Active & Passive surveillance mechanism for adverse events
- Consider two doses of VV and post vaccination serology to guide MMR doses



Clinical Protocols:

Use of LAVV post-transplant



Research

- Identify barriers and facilitators to implementation of clinical protocol
- Evaluate safety and immunogenicity of LAVV given according to clinical protocol

Optimizing Varicella Immunization in Children with SOT
SIC Network

Criteria for use of LAVV in pediatric SOT recipients Stollery Children's Hospital

>1 year **post-liver or renal** transplant

Clinically stable

Negative VZV serology and <2 doses of LAVV

Minimal immunosuppression

Immune investigations normal for age

- Total lymphocyte count
- CD4+ T cell count
- Serum IgG

Reliable follow-up for potential adverse events

Monitoring Post Vaccination



Seek medical attention promptly for new onset of rash, fever



Telephone contact 3-4 weeks after vaccination

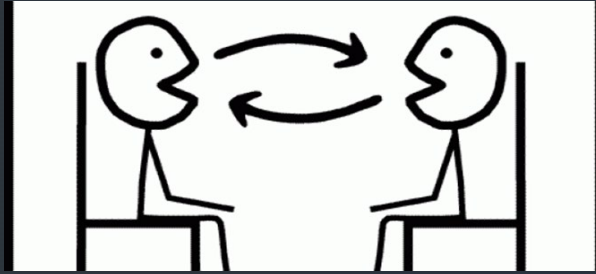
Immunization for Child SOT (after 18 months)

Alberta Immunization Policy | Special Situations for Immunization

©2022 Government of Alberta | Revision Date: February 15, 2022 | Published February 2022 | Page 1 of 8

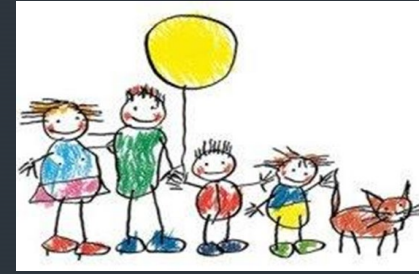


VZ	Selected pediatric renal and liver transplant recipients	The use of live univalent varicella vaccine has been shown to be safe and effective in carefully selected pediatric renal and liver transplant recipients >1 year post-transplant receiving minimal immune suppression. In consultation with the transplant team (transplant/infectious disease physician), univalent varicella vaccine may be administered to select pediatric renal and liver transplant recipients without recent graft rejection and receiving minimal immune suppression who were not optimally immunized prior to transplant. ^{1,5}
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Healthcare Provider Interviews

- Views and experiences regarding **live** and **non-live** vaccines before and after SOT
- Barriers to implementing immunization guidelines
 - Possible solutions



Parent & Patient Interviews

- Willingness to receive LAVV if recommended by transplant team
- Impact of possible VZV exposures on the child and family's lives

Communicating Changing Recommendations

Healthcare providers need to understand and communicate to families how and why guidelines and recommendations change over time

Trust between healthcare providers and families facilitates communication

Information about new guidelines or evidence should be communicated in a family- and child-specific way that resonates with parents' role as leaders

Evaluate safety and immunogenicity of LAVV given according to clinical protocol

- 59 pediatric SOT recipients vaccinated with LAVV
- Learning along the way
 - Many in the “Yellow light: caution with live vaccines” category
 - Update clinical pathways to better address this

Potential Impact

- Inform implementation of protocols for use of LAVV in pediatric SOT recipients across Canada
 - Educational Materials to support Implementation



Individualizing vaccine recommendations for immunocompromised individuals

Immunization in Immunocompromised Individuals is complex!

- Balance
 - clear guidelines/schedules
 - flexibility to individualize recommendations
 - risks of avoiding/delaying vaccines due to safety/efficacy concerns
 - risks of susceptibility to vaccine preventable diseases



Case for thought

- 8 year old boy, liver transplant at 7 months of age
 - No varicella or MMR vaccines prior to transplant
- Determined to be eligible to receive LAVV
 - positive varicella IgG 8 weeks after second dose of LAVV
 - No AEFI
- His family is planning a long trip to India and wonder if their son could get MMR vaccine

Live vaccines after pediatric solid organ transplant: Proceedings of a consensus meeting, 2018

- In low-incidence areas, recommend restriction of MMR vaccination after transplantation to local outbreaks or planned travel to high-incidence areas

Original Investigation | Infectious Diseases

Safety and Immunogenicity of Live Viral Vaccines in a Multicenter Cohort of Pediatric Transplant Recipients

- 236 pediatric SOT recipients (96% liver) received MMR vaccine
- 86% developed protective measles antibodies
- No serious adverse events

Case for thought (2)

- 7 month old female being assessed for a heart transplant
- Cardiac surgery 3 months ago
 - received packed red blood cells
- The heart transplant team plans to list her for transplant in 6 weeks
- They ask if she should receive MMR and Varicella vaccines now?

- Potential for passive antibody to interfere with response to MMR and LAVV
 - Young age
 - Recent blood products
- May be the only opportunity for MMR and LAVV
 - given >4 weeks prior to transplant
 - Less evidence to support use post-transplant in heart transplant recipients

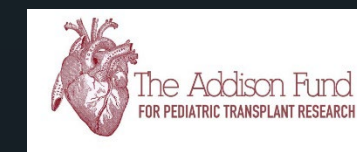


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- Chris Bon
- Elaine Yong



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Thank you!