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OIAC Ontario Immunization Advisory Committee
CCOI Comité consultatif ontarien de l'immunisation

Summary of Recommendations: Measles Post-Exposure Prophylaxis for Individuals Who Are Immunocompromised Due to Disease or Therapy

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This document summarizes Ontario Immunization Advisory Committee (OIAC) recommendations detailed in the statement, Recommendations: Measles Post-Exposure Prophylaxis for Individuals Who Are Immunocompromised Due to Disease or Therapy[1] and has been reformatted from the original version. These recommendations are not intended to be prescriptive and should only be used as a guide.

Group	Definition	Measles Susceptibility Assessment	Time Since Exposure: ≤72 Hours (≤3 Days)	Time Since Exposure: 73 Hours – 6 Days
Group A: Individuals with an absence or near-absence of a functioning immune system	**1. Transplant**[a] • Within 12 months of receiving autologous hematopoietic stem cell transplant (HSCT) or 24 months of receiving allogeneic HSCT or those with chronic graft-versus-host disease • Within 12 months of a solid organ transplant **2. Chimeric antigen receptor (CAR) T-cell therapy** • Within 12 months of undergoing CAR T-cell therapy for malignancy **3. Acute lymphoblastic leukemia**[a] • Acute lymphoblastic leukemia within and until 3 months after completion of chemotherapy or 12 months after completion of B cell depleting therapy **4. Human immunodeficiency virus (HIV) infection**[b] • HIV infection with a current CD4 T cell count <15% (age 1 – 13 years) or <200 cells/mm^3 (age ≥14 years), or a CD4:CD8 ratio <0.5 (adults) **5. Primary immunodeficiency** • Significant primary immunodeficiency or inborn error of immunity (e.g., X-linked agammaglobulinemia, severe combined immunodeficiency, severe antibody deficiency, ataxia-telangiectasia, select defects in intrinsic and innate immunity, etc.) for which live viral vaccines are contraindicated[c,d] **6. Therapies/medications** • Receiving cyclophosphamide or anti-thymocyte globulin • Receiving or completed alemtuzumab or B cell depleting (e.g., rituximab) treatment within the past 12 months[a]	Assume individual is susceptible regardless of year of birth, prior lab-confirmed measles infection, or measles vaccination status	IMIg (bodyweight <30kg) or IVIg (bodyweight ≥30 kg) MMR vaccine is contraindicated	IMIg (bodyweight <30kg) or IVIg (bodyweight ≥30 kg) MMR vaccine is contraindicated

Group	Definition	Measles Susceptibility Assessment	Time Since Exposure: ≤72 Hours (≤3 Days)	Time Since Exposure: 73 Hours – 6 Days
Group B: Individuals who may be able to maintain adequate immunity from past infection or vaccination	**1. Transplant**[a] • >12 months but <24 months post autologous HSCT • >12 months post solid organ transplant **2. CAR T-cell therapy** • >12 months post CAR T-cell therapy[e] **3. Malignancy** • Lymphoproliferative diseases including hematologic cancers (e.g., indolent lymphoma, leukemia or plasma cell lymphoma) except for acute lymphoblastic leukemia • Immunotherapy/targeted cancer therapy/chemotherapy/radiotherapy for malignancy other than acute lymphoblastic leukemia (e.g., solid tumour or hematologic including multiple myeloma) that is ongoing or completed within the last 3 months **4. Secondary immunodeficiency** • Secondary (non-congenital) hypogammaglobulinemia due to disease (e.g., nephrotic syndrome) or therapy (e.g., chemotherapy)[c] **5. Therapies/medications** • Targeted immunosuppressive therapies not mentioned above including cytokine inhibitors (e.g., tumor necrosis factor, IL-1, IL-12/23, IL-17, IL-23), costimulation modulators, and small molecule inhibitors (e.g., JAK inhibitors), alone or in combination with steroids or other immunosuppressive drugs, that are ongoing or received <6 months prior to exposure[f] • Ongoing, <4 weeks since completion, or tapering following daily corticosteroid therapy at a prednisone or equivalent dose of ≥20 mg/day for ≥14 days for adults. High-dose prednisone thresholds for children vary across guidelines and range from ≥0.5 mg/kg/day to ≥2 mg/kg/day.[g] • Ongoing or within 3 months of completing treatment with immunosuppressive drugs for immune-mediated diseases (e.g., methotrexate >0.4 mg/kg/week [children: >10 mg/m^2/week; adults: >15 mg/m^2/week], azathioprine >3 mg/kg/day, 6-mercaptopurine >1.5 mg/kg/day, cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil, and small molecule inhibitors)[f]	An individual's susceptibility and need for Ig PEP should be examined regardless of their year of birth, prior lab-confirmed measles infection, or measles vaccination status. • If available, consider rapid measles IgG serology testing if not performed recently.[h] IVIg/IMIg for measles PEP is not recommended for those with a positive measles IgG result after becoming immunocompromised.[i] • If serology is negative or timely measles IgG serology testing is not available (i.e., would not permit administration of Ig within the 6-day window), evaluate the risks versus benefits of PEP, ideally with input from the specialist responsible for the clinical care of the individual or in consultation with an infectious disease expert/immunologist. Risk-benefit assessment should also consider the duration and intensity of measles exposure (e.g., household contact).	IMIg (bodyweight <30kg) or IVIg (bodyweight ≥30 kg) MMR vaccine is not recommended[j]	IMIg (bodyweight <30kg) or IVIg (bodyweight ≥30 kg) MMR vaccine is not recommended[j]

Group	Definition	Measles Susceptibility Assessment	Time Since Exposure: ≤72 Hours (≤3 Days)	Time Since Exposure: 73 Hours – 6 Days
Group C: Susceptible individuals with only low-level immunosuppression or only mild immunocompromising conditions[k]	**1. Transplant** • >24 months following HSCT with no chronic graft-versus-host disease **2. HIV infection[b]** • Asymptomatic HIV-infected patients with CD4 T cell counts ≥15% (age 1 – 13 years) or ≥200 cells/mm^3 (age ≥14 years) with a CD4:CD8 ratio ≥0.5 (adults) **3. Primary immunodeficiencies** • Minor B cell deficiency with intact T cell function not requiring Ig therapy, partial T cell defects, and other primary immune deficiencies or inborn error of immunity for which live viral vaccines are not contraindicated[d] **4. Therapies/medications** • Prednisone or equivalent doses <20 mg/day for adults taken for ≥14 days or receiving alternate day corticosteroid therapy. For children, prednisone thresholds vary from <0.5 mg/kg/day to <2 mg/kg/day across different guidelines[g] • ≥4 weeks after discontinuation of long-term (≥14 days) high-dose systemic steroids, or immediately after discontinuation of high-dose steroids taken for <14 days[g] • Therapies that target immune system components, but are unlikely to impair immune pathways involved in infection prevention or control (e.g., anti-IgE, cytokine inhibitors used in the treatment of atopic dermatitis/asthma) • Methotrexate ≤0.4 mg/kg/week (children: ≤10 mg/m^2/week; adults: ≤15 mg/m^2/week) • Azathioprine ≤3 mg/kg/day[l] • 6-mercaptopurine ≤1.5 mg/kg/day • Hydroxychloroquine (any dose)	For HSCT recipients, assume individual is susceptible unless vaccinated post HSCT and have adequate measles antibody titres. For all other groups except HSCT recipients, assume individual is immune if born before 1970—measles PEP is not recommended for individuals with mildly immunocompromising conditions who are in this age group. Measles PEP should be offered to susceptible individuals born in or after 1970 without at least one of the following [m,n,o]: • Documented evidence of vaccination with 2 valid doses of measles-containing vaccine • Positive measles IgG serology[h] • Documented evidence of past lab-confirmed measles infection	MMR vaccine	MMR vaccine is not intended to provide protection as PEP, but should be offered to provide long-term protection[p]

Notes: CAR, chimeric antigen receptor; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplant; IgE, immunoglobulin E; IgG, immunoglobulin G; IL-1, interleukin; IL-12, interleukin 12; IL-17, interleukin 17; IL-23, interleukin 23; IMIg, intramuscular immunoglobulin; IVIg, intravenous immunoglobulin; JAK, Janus kinase; MMR, measles, mumps and rubella; PEP, post-exposure prophylaxis.

[a] Immune reconstitution is progressive and may occur sooner than the timeframe indicated. Consultation with the specialist responsible for the clinical care of the individual is recommended.

[b] Individuals with uncontrolled HIV viral loads may be at increased risk of measles complications and may not maintain an adequate immune response to the MMR vaccine. Consultation with the specialist responsible for the clinical care of the individual is recommended.

[c] It takes approximately 3–4 months for IgG levels to reach a steady state in individuals receiving regular immunoglobulin replacement. Individuals with severe primary immunodeficiency or secondary hypogammaglobulinemia on regular immunoglobulin replacement therapy for >4 months do not require additional IVIg for PEP. Consult the specialist responsible for the clinical care of the individual or an infectious disease expert/immunologist if exposure occurs <4 months since the initiation of immunoglobulin replacement therapy. NACI and CDC offer guidance for individuals on Ig replacement therapy.[2,3]

[d] As per the Canadian Immunization Guide, the MMR vaccine is contraindicated in individuals with: major B cell deficiency, severe combined B and T cell immunodeficiency, severe T cell deficiency, leukocyte adhesion defects, Chediak-Higashi syndrome and other defects in cytotoxic granule release, undefined phagocyte defect, defects in alpha or gamma interferon production, and nuclear factor kappa B defects. In addition, MMR vaccine is not recommended for individuals receiving regular Ig replacement therapy.[4]

[e] The timeframe for immune reconstitution following CAR T-cell therapy is variable. Consultation with the specialist responsible for the clinical care of the individual is recommended.

[f] Interval from treatment completion may vary with the type and intensity of treatment. Period may be shortened for biologics/treatments with a shorter duration of effect.

[g] For children, a prednisone dose of 20 mg/day is often equivalent to doses below 2 mg/kg/day. There is no consensus regarding the lowest prednisone or equivalent dose that would be considered immunosuppressive in children; thresholds vary across various guidelines from ≥0.5 mg/kg/day to ≥2 mg/kg/day.[4-6]

[h] To inform PEP decisions, measles IgG serology should either: 1) be done following measles exposure through rapid testing, or 2) have been done prior to measles exposure, but AFTER the individual became immunocompromised. Clinical judgement should be used to determine the suitability of past measles IgG serology, if available.

[i] Results of measles immunity serology from Public Health Ontario are reported as reactive (positive), indeterminate, or non-reactive (negative).

[j] The MMR vaccine may be given in some circumstances in consultation with an infectious disease expert/immunologist. The MMR vaccine is not intended to provide protection as PEP if given >3 days post-exposure; if given >3 days post-exposure, its role is to provide long-term protection.

[k] This guidance document does not provide a comprehensive list of mild immunocompromising medical conditions or therapies that result in low-level immunosuppression. Medications that induce low-level immunosuppression may result in a greater degree of immunosuppression when combined. Assessment of severity of immunocompromising condition is often best determined by consulting with the treating physician, infectious disease, expert/immunologist, or special immunization clinic.

[l] Individuals on azathioprine exhibiting signs of myelosuppression/myelotoxicity should be assessed for susceptibility and need for Ig PEP. Please refer to guidance for ‘Individuals who may be able to maintain adequate immunity from past infection or vaccination‘.

[m] Individuals born before 1970 are generally considered to have presumptive immunity with some exceptions (i.e., healthcare workers).[3,7]

[n] Individuals with unknown measles immunization status should be considered susceptible unless they meet at least one of the other two immune criteria (i.e., measles IgG positive or documented past lab-confirmed measles infection).

[o] In Canada, adults born before 1970 are generally presumed to have acquired immunity through past infection due to high levels of measles circulation up until the 1960s. With the exception of the United States where a birth year threshold of 1957 is used, other countries have had endemic measles circulation until 1970 or later. For this reason, the 1970 birth year threshold can also be applied to individuals born and raised outside of Canada, with the exception of the United States.

[p] Individuals with low-level immunosuppression are managed similarly to immunocompetent contacts who are not recommended to receive Ig as measles post-exposure prophylaxis unless they are under the age of 12 months or susceptible pregnant individuals.

References

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About the Ontario Immunization Advisory Committee

The Ontario Immunization Advisory Committee (OIAC) was established in August 2021 at the request of the Chief Medical Officer of Health. The Committee provides scientific and technical advice to Public Health Ontario on vaccines and immunization matters, including program implementation in Ontario, priority populations, clinical guidance, and vaccine safety and effectiveness.

OIAC's work focuses on publicly funded vaccines and immunization programs in Ontario, and those under consideration for new programming. The OIAC provides advice by applying scientific knowledge and the best available evidence, in addition to feasibility, acceptability and other implementation considerations.

For more information about the OIAC and its members contact secretariat@oahpp.ca.

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