RAPID COMMUNICATION

Updated NACI recommendations for measles post-exposure prophylaxis

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Abstract

Background: Human immune globulin (Ig) products are currently recommended as post-exposure prophylaxis (PEP) for measles in certain susceptible groups. However, successful measles vaccination programs in North America have led to low circulation of measles virus and most blood donors now have vaccine-derived immunity. Concurrently, the concentrations of anti-measles antibodies in human Ig products have shown trends of gradual decline and previously recommended doses and routes of administration may no longer be optimally protective.

Objectives: To review the literature and update recommendations on post-exposure prophylaxis for measles, including dosing and route of administration, for measles Ig PEP in susceptible infants and in individuals who are immunocompromised or pregnant, in order to prevent severe disease.

Approach: The National Advisory Committee on Immunization (NACI) Measles, Mumps, Rubella, Varicella Working Group reviewed key literature, international practices, and product information for current Ig products pertaining to the optimal dosage and routes of Ig administration for measles PEP. It then proposed evidence-based changes to the PEP recommendations that were considered and approved by NACI.

Results: NACI continues to recommend that susceptible immunocompetent individuals six months of age and older, who are exposed to measles and who have no contraindications be given measles-mumps-rubella (MMR) vaccine within 72 hours of the exposure. NACI recommends that for susceptible infants younger than six months of age, if injection volume is not a major concern, intramuscular immunoglobulin (IMIg) should be provided at a concentration of 0.5 mL/kg, to a maximum dose of 15 mL administered over multiple injection sites. Susceptible infants six to 12 months old who are identified after 72 hours and within six days of measles exposure should receive IMIg (0.5 mL/kg) if injection volume is not a major concern. For susceptible contacts who are pregnant or immunocompromised, if injection volume is not a concern, IMIg can be provided at a concentration of 0.5 mL/kg understanding that recipients 30 kg or more will not receive the measles antibody concentrations that are considered to be fully protective. Alternatively, in cases where injection volume is a major concern or for recipients 30 kg or more, intravenous immunoglobulin (IVIg) can be provided at a dose of 400 mg/kg.

NACI does not recommend that susceptible immunocompetent individuals older than 12 months of age receive Ig PEP for measles exposure due to the low risk of disease complications and the practical challenges of administration for case and contact management.

Conclusion: NACI has updated the recommendations for measles PEP to reflect current evidence and best practices in order to prevent severe disease in Canada. Consistent with recommendations in other countries, this includes consideration of off-label use of IVIg in some instances.

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Introduction

Although Canada has maintained measles elimination status since 1998, sporadic measles activity continues to occur on occasion, typically among susceptible individuals. Recent measles activity in Canada and the declining potency of immune globulin (Ig) products over time has led to a review of the National Advisory Committee on Immunization (NACI) recommendations for measles post-exposure prophylaxis (PEP).

Intramuscular immunoglobulin (IMIg) products have previously been recommended by NACI for measles PEP in susceptible

contacts who are pregnant or immunocompromised, children younger than six months of age and susceptible immunocompetent contacts six months or older who present to a health care professional more than 72 hours but within six days after measles exposure (1). Susceptible individuals are those who do not meet the criteria for measles immunity outlined in the Canadian Immunization Guide in guidelines for the prevention and control of measles outbreaks in Canada (1).

Over the past fifty years, successful measles vaccination programs in North America have led to low circulation of measles virus and absence of natural infection. Concurrently, the concentrations of anti-measles antibodies in human Ig products have shown trends of gradual decline and are no longer considered optimally protective, using the previously recommended doses and routes of administration (2).

Although the exact protective level of anti-measles antibody is not known, an anti-measles titre of >120 milli International Units per millilitre (mIU/mL) of serum is generally considered to be protective and has been associated with protection in healthy young adults (3). Human Ig products are authorized in Canada for use as measles PEP based on compliance with the Center for Biologics Evaluation and Research (CBER) reference standard that was issued from the United States of America (USA) Food and Drug Administration (FDA) in 2006 (4,5). In light of this product information, NACI reviewed key evidence sources in order to revise recommendations on measles PEP dosage and routes of administration.

The objective of this update is to revise recommendations on measles PEP in response to recent measles activity in Canada and the declining potency of Ig products over time. There is no full NACI Statement on this topic, but changes are reflected in the Canadian Immunization Guide (6) and NACI will provide a comprehensive review of measles PEP in a future statement.

Methods

The NACI Measles, Mumps, Rubella, Varicella Working Group (MMRVWG) reviewed key literature, international practices, and evidence from manufacturers pertaining to the optimal dosage and routes of Ig administration for measles PEP. Key literature was identified through an environmental scan of international recommendations and practices, including National Immunization Technical Advisory Groups from the USA (Advisory Committee on Immunization Practices), the United Kingdom (UK) (Joint Committee on Vaccination and Immunization), Germany (Standing Committee on Vaccination), Australia (Australian Technical Advisory Group on Immunization), France (Technical Vaccination Committee), New Zealand and Ireland. Once key studies were identified, their references were searched for additional pertinent studies. In total, six relevant reference studies were identified (3,4,7–9). In addition, data were presented to the MMRVWG from the intramuscular immunoglobulin (IMIg) manufacturer, Grifols, on the state of anti-measles concentration in products over the years, as well as available evidence on anti-measles antibody concentrations in recipients of the Ig products at different dosages and routes of administration.

Results

Following a review of international practices, product information for current Ig products and key literature, the MMRVWG considered the effectiveness, appropriate dosing and optimal administration routes for Ig products to protect against measles in vulnerable and susceptible populations. Results are presented below as they pertain to the route of administration: intramuscular or intravenous.

In order to interpret key effectiveness literature, each study had to be evaluated in relation to the concentration of anti-measles antibodies in today's Ig products according to a common reference standard. The current minimum concentration requirement for anti-measles antibodies in Ig preparations is 0.60 x CBER Reference Standard #176 (42 IU/mL) (4), which is equivalent to 25 IU/mL. Data presented to the NACI MMRVWG by Grifols, the manufacturer of both the IMIg product GammaSTAN® (10) and the intravenous immunoglobulin (IVIg) product Gamunex® (11), suggested that the anti-measles antibody levels are declining over years but are still well above the minimum regulatory threshold. Recent measurements (2015–2016) have been in the range of 0.79 x CBER Reference Standard, which is equivalent to 33 IU/mL. Although not all IVIg manufacturers presented data, all Ig preparations available in Canada contain pooled plasma from USA donors, except IGIVnex®, which contains plasma from Canadian donors. Therefore, it can be reasonably assumed, that trends in antibody concentration would be reflected across products.

There is no simple or reliable way to predict serum anti-measles titres based on the PEP dosage administered. Previous attempts have used mathematical estimations and modelling, including those outlined by Audet et al. in 2006, to establish the CBER reference standard in relation to a threshold of 120 mIU/mL (4). Real world effectiveness studies for IMIg measles PEP are more useful, but there are very few relevant effectiveness studies (7–9).

Intramuscular immunoglobulin

Available evidence and product information was reviewed concerning IMIg, which has previously been recommended by NACI for measles PEP at a dose of 0.25 mL/kg for susceptible pregnant women and infants or 0.5 mL/kg for immunocompromised individuals, or for other susceptible contacts who presented between 72 hours and six days post-exposure. GammaSTAN (10) is the only IMIg preparation in Canada, and it is indicated for use as measles PEP. When effectiveness studies were examined based on the relative anti-measles antibody concentrations in current Ig products, it was apparent that IMIg doses exceeding the CBER Reference Standard with current protein concentrations of 0.442 mL/kg, 0.393 mL/kg or 0.335 mL/kg, would result in 100%, 100% and 83% effectiveness respectively against measles up to two weeks post-injection (9). Dosing equivalent to 0.297 mL/kg in current products would result in an estimated 69% effectiveness (7), while dosing equivalent to 0.157 mL/kg showed only 42.9% effectiveness against measles up to two weeks post-injection (9). A study by Sheppeard et al. found that a dose of 0.19ml/ kg by today's equivalent products would result in effectiveness of 75.8%, but this study was considered to have a high risk of effectiveness overestimation based on a broad definition

of exposure to measles cases (8). It should be noted that the sample sizes for all of these studies were small; ranging from 1–55 subjects receiving various dosages of IMIg.

Despite the limited evidence, it is assumed that IMIg at the previously recommended dosing of 0.25 mL/kg for susceptible pregnant women and infants is not fully protective against measles, even though these products do exceed the current CBER Reference Standard. Given the available effectiveness data and the emerging trend towards diminishing concentration of anti-measles antibodies within North American products, the MMRVWG determined that an IMIg dose of 0.5 mL/kg would be appropriate to provide immediate protection at current product concentrations of anti-measles antibody, and also to mitigate against future declining potency of the Ig products. IMIg can be provided up to a maximum volume of 15 mL, therefore anyone weighing 30 kg or more will not receive an optimal dose of IMIg at 0.5 mL/kg. Large volumes (greater than 2 mL for children or 3–5 mL for adults) should be divided and injected at two or more sites (12); therefore, anyone receiving 15 mL of IMIg would be subject to multiple injections. Multiple injections may not be acceptable to all patients, and IVIg may therefore be preferred.

Intravenous immunoglobulin

Although IVIg preparations are not indicated in Canada for use as measles PEP, the MMRVWG considered the use of IVIg as an alternative strategy based on international practices and the lack of alternative prophylaxis strategies. Gamunex IVIg is in fact indicated for measles PEP by the FDA in the USA. Moreover, several countries routinely use IVIg preparations for measles PEP in immunodeficient or immunosuppressed populations, or in circumstances where a large dose would be required, including the USA (13), UK (14), New Zealand (15), Ireland (16) and France (17). Although IVIg is not indicated for measles PEP in Canada, NACI determined that it is an important strategy to prevent post-exposure measles disease in susceptible and vulnerable groups, particularly individuals weighing more than 30 kg. Subcutaneous dosing is rarely used, and following discussion NACI identified significant logistical barriers to subcutaneous administration, including an infusion pump and advanced training.

For IVIg administration, 400 mg/kg is a standard dosage that is within the indicated range of Ig replacement therapy for patients with primary immunodeficiency according to Canadian product monographs for Gammagard® (18,19), Gamunex (11), IGIVnex (20), Privigen® (21) and Panzyga® (22) which are the IVIg products available in Canada through Canadian Blood Services (CBS). Although there is no maximum infusion volume listed in the product monographs, reactions can be prevented in many cases by slowing the infusion rate (23). Maximum infusion rates have been summarized by CBS (24).

Unpublished data on file from Grifols indicates that the serum levels of anti-measles antibodies in 10 children aged 2–16 years with primary immunodeficiency who received Gamunex IVIg at doses ranging from 300–600 mg/mL were all more than four-fold higher than the 120 mIU/mL protective level for measles. Individuals already receiving replacement IVIg at 400 mg/kg of body weight or higher are therefore considered protected against measles and do not require Ig if the last dose of IVIg was received within three weeks prior to measles exposure.

IVIg necessitates administration in the hospital and active patient monitoring over several hours of infusion, performed by appropriately-trained staff (23). In remote settings, IVIg administration can require evacuation by air to a larger medical centre. Although there are implementation barriers to intravenous administration, it may be preferable in some cases as an alternative to multiple IM injections or to ensure an optimal protective dose for susceptible vulnerable individuals who require more than 15 mL of IMIg.

CBS is the supplier of IMIg and IVIg blood products in Canada. It is advisable that providers review the respective product monographs and CBS guidelines (23,24) prior to administering IVIg products for information on administration practices, adverse events and repeated administration. The safety of these products is monitored and reviewed by Health Canada, CBS (25), and Public Health Agency of Canada (PHAC) Blood Safety Contribution Program, which includes the Transfusion Transmitted Injuries Surveillance System (27). Further information on the administration of passive immunizing agents can be found in the Canadian Immunization Guide.

Recommendations

NACI continues to recommend that susceptible immunocompetent individuals six months of age and older who are exposed to measles and who have no contraindications, be given measles-mumps-rubella (MMR) vaccine within 72 hours of the exposure. NACI recommends that for susceptible infants younger than six months of age, if injection volume is not a major concern, IMIg should be provided at a concentration of 0.5 mL/kg, to a maximum dose of 15 mL administered over multiple injection sites. Susceptible infants six to 12 months old who are identified after 72 hours and within six days of measles exposure should receive IMIg (0.5 mL/kg) if injection volume is not a major concern. For susceptible contacts who are pregnant or immunocompromised, if injection volume is not a concern, IMIg can be provided at a concentration of 0.5 mL/kg, understanding that recipients weighing 30 kg or more will not receive the measles antibody concentrations that are considered to be fully protective. In cases where injection volume is a major concern or for recipients weighing 30 kg or more, IVIg can be provided alternatively at a dose of 400 mg/kg.

NACI does not recommend that susceptible immunocompetent individuals older than 12 months of age receive Ig PEP for measles exposure due to low risk of disease complications and the practical challenges of administration for case and contact management. **Table 1** includes an updated summary of recommended measles PEP strategies.

Table 1: Summary of updated measles post-exposure prophylaxis recommendations for susceptible contacts

Population	Time since exposure to measles[a]	
	≤ 72 hours	73 hours–six days
Susceptible infants 0–6 months of age[b]	IMIg (0.5 mL/kg)[c]	
Susceptible immunocompetent infants 6–12 months of age	MMR vaccine[d]	IMIg (0.5 mL/kg)[b,e]

Table 1: (continued) **Summary of updated measles post-exposure prophylaxis recommendations for susceptible contacts**

Population	Time since exposure to measles[a]	
	≤ 72 hours	73 hours–six days
Susceptible immunocompetent individuals 12 months of age and older	MMR vaccine series[e]	
Susceptible pregnant individuals[f]	IVIg (400 mg/kg) or IMIg (0.5 mL/kg), limited protection[g]	
Immunocompromised individuals six months of age and older	IVIg (400 mg/kg) or IMIg (0.5 mL/kg), limited protection if 30 kg or more[g]	
Individuals with confirmed measles immunity	Not applicable	

Abbreviations: IMIg, intramuscular immunoglobulin; IVIg, intravenous immunoglobulin; MMR, measles-mumps-rubella
[a] Ig should only be provided within six days of measles exposure. Individuals already receiving replacement IVIg (400 mg/kg of body weight or higher) are considered protected against measles and do not require Ig if the last dose of IVIg was received within three weeks prior to measles exposure
[b] Two doses of measles-containing vaccine are still required after the first birthday for long-term protection
[c] If injection volume is a major concern, IVIg can be provided at a concentration of 400 mg/kg
[d] Two additional doses of MMR vaccine provided after 12 months of age are required for long term protection
[e] MMR vaccine will not provide PEP protection after 72 hours of exposure, however, starting and completing a two dose series should not be delayed to provide long term protection
[f] Provide two doses of MMR vaccine postpartum for long-term protection
[g] For individuals weighing 30 kg or more, IMIg will not provide complete protection but may provide partial protection

Discussion and conclusion

NACI has updated the recommendations for measles PEP to reflect current evidence and best practices in order to prevent severe disease. NACI continues to recommend that PEP should be considered for select susceptible or vulnerable groups within six days of measles exposure. Susceptible individuals who are not infants, pregnant or immunocompromised, are no longer recommended to receive Ig following measles exposure. Although IVIg products are not indicated for use as measles PEP in Canada, NACI now recommends them as an alternative to IMIg because there are no comparable appropriate prophylaxis strategies in some situations.

NACI provides PHAC with ongoing and timely medical, scientific and public health advice relating to immunization. PHAC acknowledges that the advice and recommendations set out in this statement are based upon the best current available scientific knowledge and is disseminating this document for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monographs. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturers have sought approval of the products and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs.

Authors' statement

MCT – Writing – original draft, writing – review and editing
MIS – Writing – original draft, writing – review and editing
VD – Writing – original draft, writing – review and editing
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This summary was prepared by the authors and approved by NACI.

Conflict of interest

None. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

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References

1. Measles and Rubella Elimination Working Group. Guidelines for the prevention and control of measles outbreaks in Canada. Can Commun Dis Rep. 2013;39(ACS-3):1-52. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-3/

assets/pdf/meas-roug-eng.pdf https://doi.org/10.14745/ccdr.v39i00a03

2. United States Food and Drug Administration, National Institute of Allergy and Infectious Diseases. Immune Globulin Potency in the 21st Century. Rockville (MD): USFDA; 2017. 288 p. www.fda.gov/downloads/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/UCM605362.pdf
3. Chen RT, Markowitz LE, Albrecht P, Stewart JA, Mofenson LM, Preblud SR Orenstein WA. Measles antibody: reevaluation of protective titers. J Infect Dis 1990 Nov;162(5):1036–42. www.ncbi.nlm.nih.gov/pubmed/2230231. PubMed https://doi.org/10.1093/infdis/162.5.1036
4. Audet S, Virata-Theimer ML, Beeler JA, Scott DE, Frazier DJ, Mikolajczyk MG Eller N, Chen FM, Yu MY. Measles-virus-neutralizing antibodies in intravenous immunoglobulins. J Infect Dis 2006 Sep;194(6):781–9. https://doi.org/10.1086/506363. PubMed (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=16941344&dopt=Abstract)
5. United States Food and Drug Administration. About the Center for Biologics Evaluation and Research (CBER). Silver Spring (MD): USFDA; 2017. www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cber/
6. Public Health Agency of Canada. Measles vaccine: Canadian Immunization Guide: Part 4 - Active Vaccines Ottawa (ON): PHAC; 2015. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-12-measles-vaccine.html#p4c11t1
7. Bigham M, Murti M, Fung C, Hemming F, Loadman S, Stam R Van Buynder P, Lem M. Estimated protective effectiveness of intramuscular immune serum globulin post-exposure prophylaxis during a measles outbreak in British Columbia, Canada, 2014. Vaccine 2017 May;35(20):2723–7. https://doi.org/10.1016/j.vaccine.2017.03.069. PubMed (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=28392140&dopt=Abstract)
8. Sheppeard V, Forssman B, Ferson MJ, Moreira C, Campbell-Lloyd S, Dwyer DE McAnulty JM. The effectiveness of prophylaxis for measles contacts in NSW. N S W Public Health Bull 2009 May-Jun;20(5-6):81–5. https://doi.org/10.1071/NB08014. PubMed (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=19552854&dopt=Abstract)
9. Endo A, Izumi H, Miyashita M, Taniguchi K, Okubo O, Harada K. Current efficacy of postexposure prophylaxis against measles with immunoglobulin. J Pediatr 2001 Jun;138(6):926–8. https://doi.org/10.1067/mpd.2001.113710. PubMed (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11391343&dopt=Abstract)
10. Grifols Therapeutics Inc. Product monograph: GamaSTAN® S/D: Immune Globulin (Human), Injectable Solution, 15-18% Protein. 2018. https://pdf.hres.ca/dpd_pm/00043801.PDF
11. Grifols Therapeutics Inc. Product monograph: GAMUNEX®: Immune Globulin Intravenous (Human), 10%. 2016. www.grifols.ca/documents/17006/298613/gamunex-ca-en.pdf/775d8f37-4376-4291-bb18-18ead549ac40
12. Public Health Agency of Canada. Canadian Immunization Guide: Part 1 - Key Immunization Information. Ottawa (ON): PHAC; [updated November 3, 2017]. www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-8-vaccine-administration-practices.html
13. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Centers for Disease Control and Prevention. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2013 Jun 14 Jun;62 RR-04:1–34. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm. PubMed (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=23760231&dopt=Abstract)
14. Public Health England. Immunization Against Infectious Disease: The Green Book. Chapter 21: Measles. London (UK):PHE; 2013. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/147968/Green-Book-Chapter-21-v2_0.pdf
15. New Zealand Blood Service Clinical Compendium. Post Exposure Prophylaxis for Measles. Auckland (New Zealand): NZBlood; 2012. www.nzblood.co.nz/assets/Transfusion-Medicine/PDFs/POST-EXPOSURE-PROPHYLAXIS-FOR-MEASLES-111G001.pdf
16. Irish Health Protection Surveillance Centre. FAQs: Preventing measles in non-immune contacts with human normal immunoglobulin (HNIG). Dublin (Ireland): HPSC; 2012. www.hpsc.ie/a-z/vaccinepreventable/measles/guidance/File,4174,en.pdf
17. Haut Conseil de la santé publique. Délai entre l'administration d'immunoglobulines après contact avec un cas de rougeole et le vaccin ROR. Paris (France): Haut Conseil de la santé publique; 2012. www.hcsp.fr/Explore.cgi/avisrapportsdomaine?clefr=267
18. Shire Pharma Canada ULC. Product monograph: GAMMAGARD LIQUID, Immune Globulin Intravenous (Human), 10%. 2018. https://pdf.hres.ca/dpd_pm/00045116.PDF
19. Shire Pharma Canada ULC. Product monograph: GAMMAGARD S/D, 5 g/vial & 10 g/vial. 2018. https://pdf.hres.ca/dpd_pm/00046330.PDF
20. Grifols Therapeutics Inc. Product Monograph: IGIVnex®. Immune Globulin Intravenous (Human), 10%. 2017. https://pdf.hres.ca/dpd_pm/00040088.PDF
21. CSL Behring Canada Inc. Product monograph: Privigen®. Immune Globulin Intravenous (Human), 10% Solution for infusion. 2018. https://pdf.hres.ca/dpd_pm/00042855.PDF
22. Octapharma. Product monograph: PANZYGA®. Immune Globulin Intravenous (Human), Solution for Infusion, 100 mg/mL. 2017. https://pdf.hres.ca/dpd_pm/00041520.PDF
23. Canadian Blood Services. Clinical Guide to Transfusion. Chapter 4: Immune Globulin Products. Ottawa (ON): CBS; 2016. https://professionaleducation.blood.ca/en/transfusion/clinical-guide/immune-globulin-products
24. Canadian Blood Services. Intravenous Immune Globulins. Ottawa (ON): CBS; 2018. https://blood.ca/sites/default/files/Intravenous_Immune_Globulins_Table.pdf
25. Canadian Blood Services. Adverse Patient Reactions. Ottawa (ON): CBS; 2018. https://blood.ca/en/hospitals/adverse-patient-reactions
26. Public Health Agency of Canada. Blood Safety Contribution Program. Ottawa (ON): PHAC; 2013. www.canada.ca/en/public-health/services/surveillance/blood-safety-contribution-program.html#ttiss