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Measles Update for Clinicians and Public Health

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May 24, 2024

Welcome and Land Acknowledgement

I acknowledge and respect the lands, sky and waters of Ontario, including for their contribution and sharing to support all life within. I acknowledge and respect the treaty, unceded and traditional territories of all First Nations across these lands and waters. I acknowledge and respect the traditional territories and communities of the Metis Nation of Ontario. I acknowledge and respect Inuit connection and contribution across these lands and waters.

Please join me in acknowledgement and respect of all Indigenous peoples, our life journeys, our worldviews, and our Indigeneity. May we respect and honour the many connections, relationships and life journeys of Indigenous peoples and our Indigeneity to the lands, sky and waters across all Ontario since time immemorial to this very day. May their wisdom always guide our own paths forward with open hands, open hearts and open minds for the mutual success and benefit of all in Ontario.

Learning Objectives

- Describe the epidemiology of measles in Ontario and globally
- Discuss case and contact management for measles, including post-exposure prophylaxis
- Measles diagnostic testing and interpretation of results
- Discuss IPAC recommendations, including PPE, for HCWs providing care for patients with suspect or confirmed measles
- Increased awareness of available key resources and guidance

Presenters

- **Sarah Wilson** is a public health physician at Public Health Ontario working supporting surveillance of vaccine-preventable diseases, immunization coverage, vaccine safety and outbreak management.
- **Maan Hasso** is a medical microbiologist at Public Health Ontario and leads the viral detection and molecular diagnostic portfolio.
- **Maureen Cividino** is an IPAC Physician with Public Health Ontario and occupational physician in acute care.

Outline

Lead	Description
Dr. Sarah Wilson	Recent Epidemiology, Clinical and Public Health Considerations
Dr. Maan Hasso	Measles Laboratory Diagnosis at PHO
Dr. Maureen Cividino	Measles IPAC update for Health Care Workers and Health Care Settings
All, facilitated by Dr. Hamidah Meghani	Q&A

Measles in Ontario: Recent Epidemiology, Clinical & Public Health Considerations

Increased Measles Activity Worldwide[1,2,3,4]

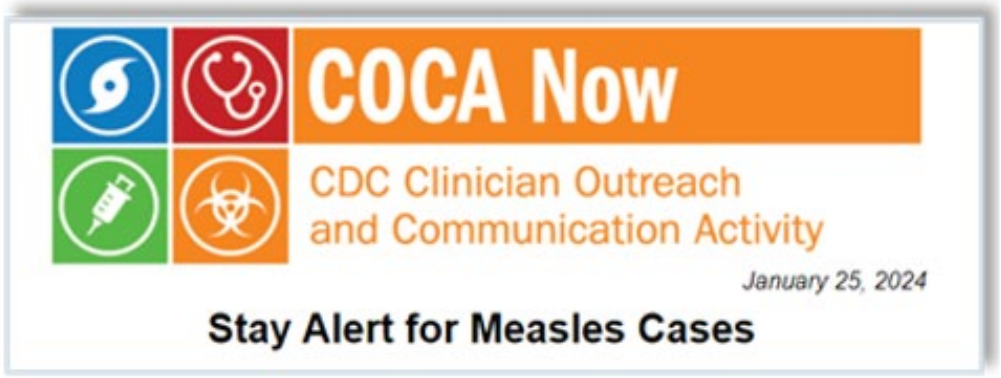
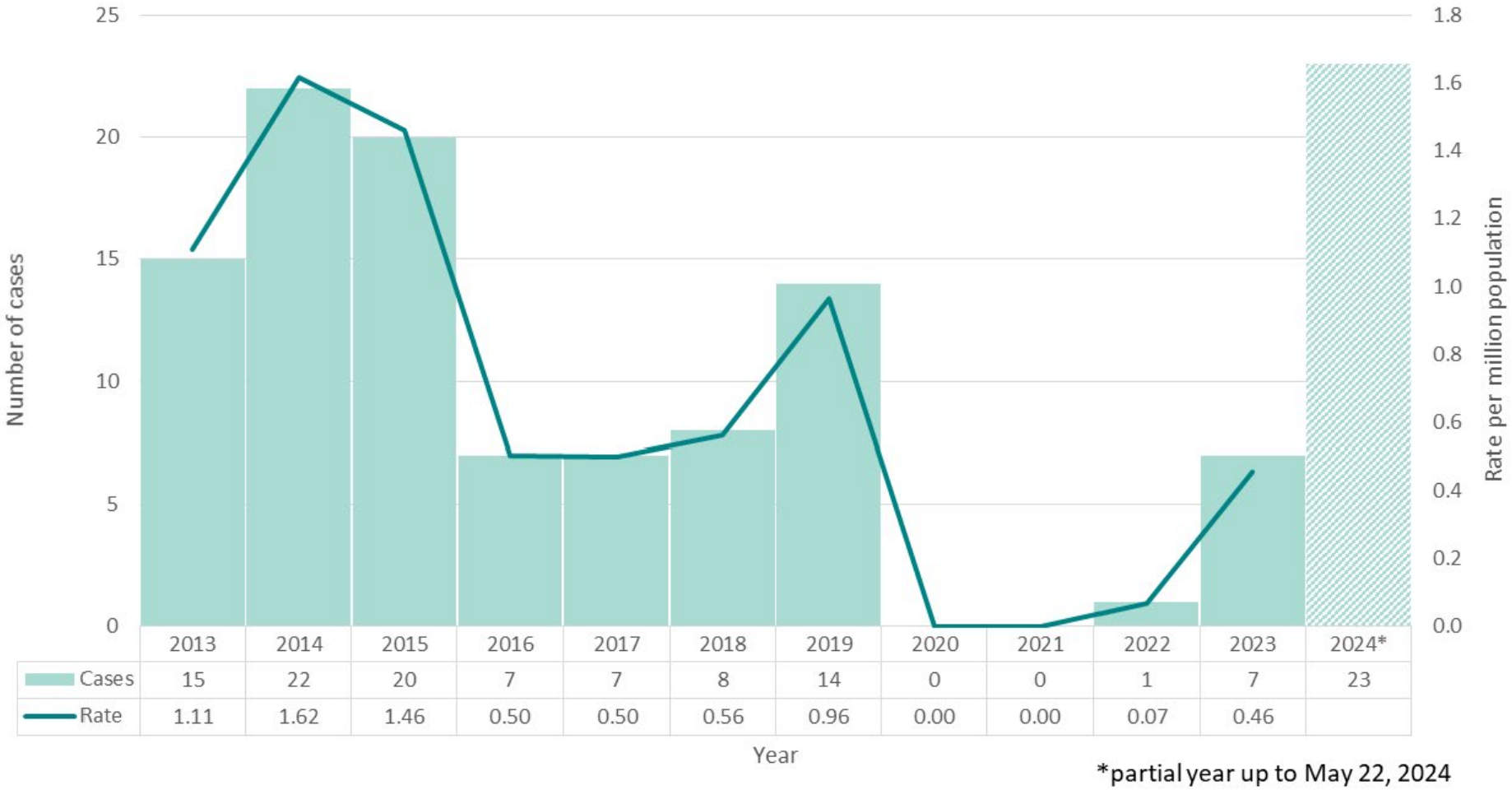


Image Sources:

1. World Health Organization (WHO). A 30-fold rise of measles cases in 2023 in the WHO European Region warrants urgent action [Internet]. Geneva: WHO; 2023 [cited 2024 May 21]. Available from: https://www.who.int/europe/news/item/14-12-2023-a-30-fold-rise-of-measles-cases-in-2023-in-the-who-european-region-warrants-urgent-action
2. European Centre for Disease Prevention and Control (ECDC). Measles on the rise in the EU/EEA: considerations for public health response [Internet]. Stockholm, ECDC; 2024 [cited 2024 May 21]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/measles-eu-threat-assessment-brief-february-2024.pdf
3. Centers for Disease Control and Prevention (CDC). Stay alert for measles cases [Internet]. Atlanta, GA: CDC; 2024 [cited 2024 May 21]. Available from: https://emergency.cdc.gov/newsletters/coca/2024/012524.html
4. Public Health Agency of Canada. Statement from the Chief Public Health Officer of Canada on global increase in measles and risk to Canada [Internet]. Press release. Ottawa, ON: Government of Canada; 2024 Feb 23 [cited 2024 May 21]. Available from: https://www.canada.ca/en/public-health/news/2024/02/statement-from-the-chief-public-health-officer-of-canada-on-global-increase-in-measles-and-risk-to-canada.html

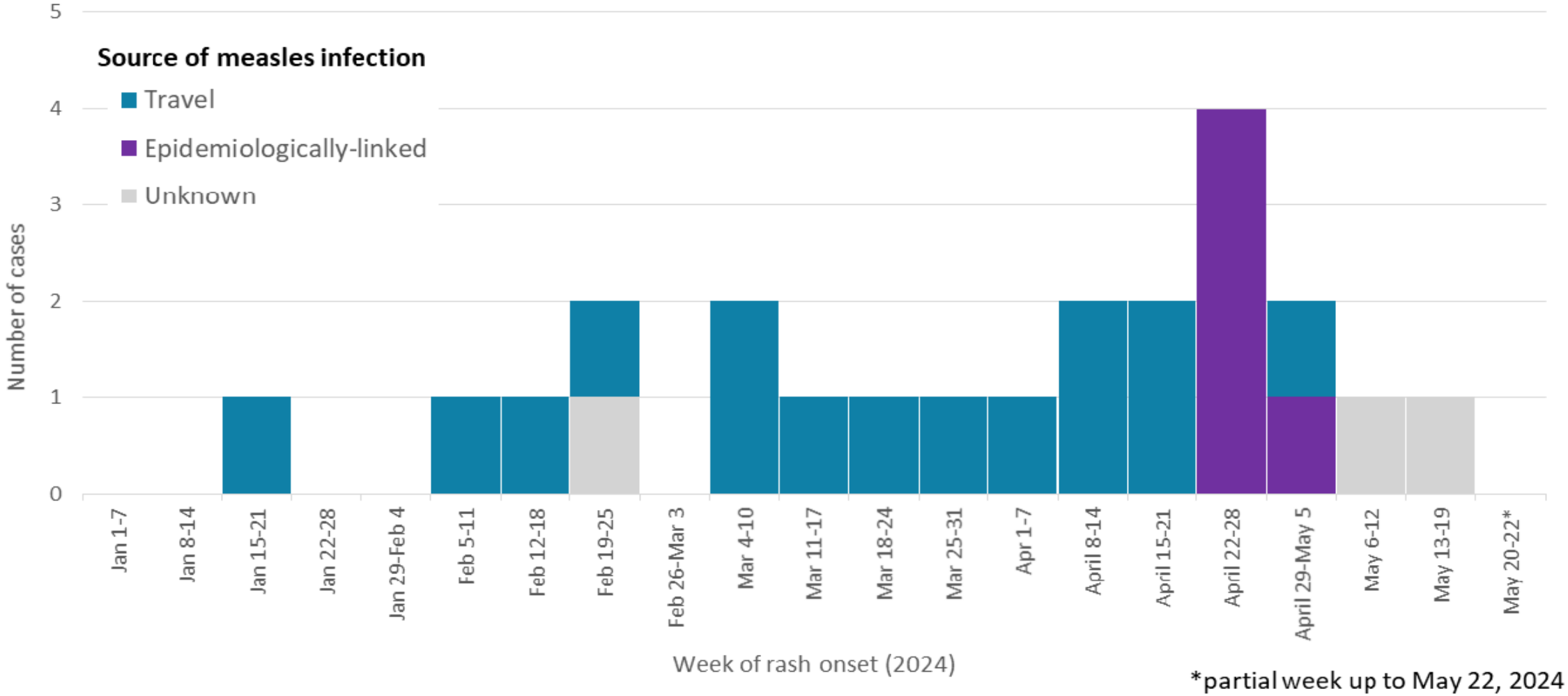
Measles in Ontario, 2013 – 2024[5]



	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Cases	15	22	20	7	7	8	14	0	0	1	7	23
Rate	1.11	1.62	1.46	0.50	0.50	0.56	0.96	0.00	0.00	0.07	0.46	

5. Ontario Agency of Health Protection and Promotion (Public Health Ontario). Measles in Ontario [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [Updated 2024 May 16; cited 2024 May 21]. Available from: https://www.publichealthontario.ca/-/media/Documents/M/24/measles-ontario-epi-summary.pdf?rev=c082f5ae0c6c446f9624d47b7e3c8535&sc_lang=en

Measles Cases in Ontario: Source of Infection[5]



5. Ontario Agency of Health Protection and Promotion (Public Health Ontario). Measles in Ontario [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [Updated 2024 May 16; cited 2024 May 21]. Available from: https://www.publichealthontario.ca/-/media/Documents/M/24/measles-ontario-epi-summary.pdf?rev=c082f5ae0c6c446f9624d47b7e3c8535&sc_lang=en

Measles in Ontario: Demographics[5]

Case Characteristics	N (%)
Age (years)	
<1	2 (8.7%)
1 – 4	8 (34.8%)
5 – 9	4 (17.4%)
10 – 19	0 (0.0%)
20 – 39	7 (30.4%)
40+	2 (8.7%)
Cases born after 1970	23 (100.0%)
Gender: Male vs Female	12 vs 11 (52.2% vs 47.8%)

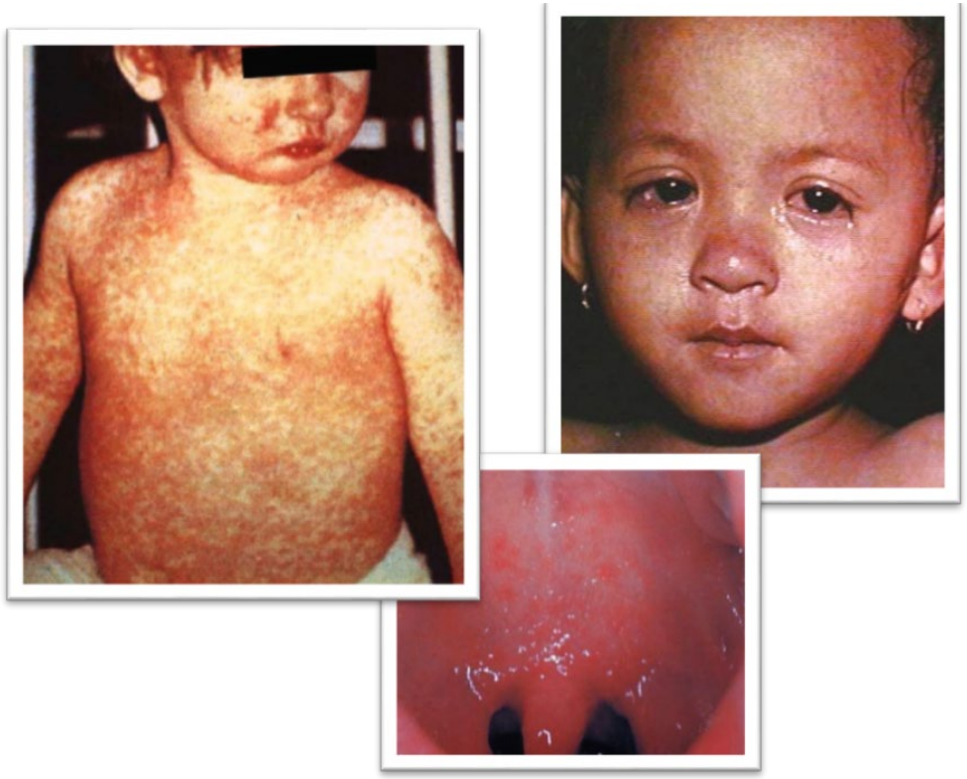
Case Characteristics	N (%)
PHUs with cases	9 of 34 (26.5%)
Hospitalized	6 (26.1%)
Deaths	1 (4.3%)
Immunization status	
Unimmunized	11 (47.8%)
1 dose	0 (0.0%)
2 or more doses	4 (17.4%)
Unknown / no proof	8 (34.8%)

5. Ontario Agency of Health Protection and Promotion (Public Health Ontario). Measles in Ontario [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [Updated 2024 May 16; cited 2024 May 21]. Available from: https://www.publichealthontario.ca/-/media/Documents/M/24/measles-ontario-epi-summary.pdf?rev=c082f5ae0c6c446f9624d47b7e3c8535&sc_lang=en

Measles: Clinical Presentation and Prevention

Clinical Presentation of Measles[6]

- Measles is characterized by:
  - Prodrome of fever
  - Cough
  - Coryza
  - Conjunctivitis
  - Maculopapular erythematous rash that begins on the face and spreads to the trunk, arms and legs
  - Koplik spots are pathognomonic
- Cases are considered infectious from 1 day before the start of the prodromal period (**4 days before to 4 days after rash onset**)

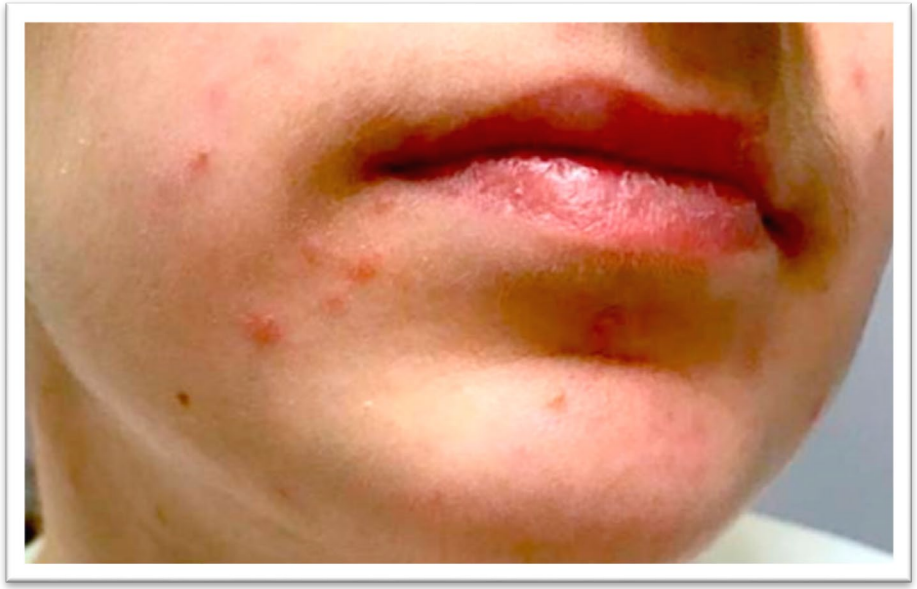


6. Public Health Agency of Canada. Measles: for health professionals [Internet]. Ottawa, ON: Government of Canada; 2024 [Updated 2024 Feb 27; cited 2024 May 21] Available from: https://www.canada.ca/en/public-health/services/diseases/measles/health-professionals-measles.html

7. Image source: Centers for Disease Control and Prevention. Photos of measles [Internet]. Atlanta, GA: 2024 [cited 2024 May 21]. Available from: https://www.cdc.gov/measles/signs-symptoms/photos-of-measles.html?CDC_AAref_Val=https://www.cdc.gov/measles/symptoms/photos.html

Vaccine-Modified Measles

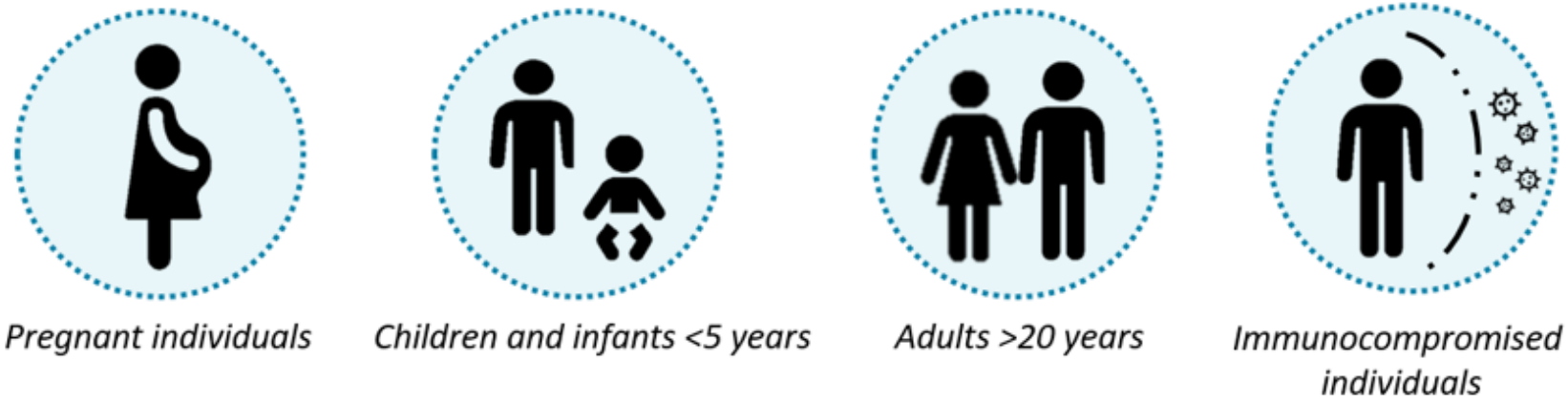
- Vaccine-modified measles is a milder form of measles in individuals who have previously been vaccinated[1]
- Symptoms are mild and some classic symptoms absent (e.g., may not have conjunctivitis, coryza or cough)[2]
- Rash may be vesicular and more localised[2]
- Lower viral load than measles infection among unvaccinated individuals[3]
- **Transmission from vaccine-modified measles cases is still possible[4]**



1. World Health Organization (WHO). A 30-fold rise of measles cases in 2023 in the WHO European Region warrants urgent action [Internet]. Geneva: WHO; 2023 [cited 2024 May 21]. Available from: https://www.who.int/europe/news/item/14-12-2023-a-30-fold-rise-of-measles-cases-in-2023-in-the-who-european-region-warrants-urgent-action
2. European Centre for Disease Prevention and Control (ECDC). Measles on the rise in the EU/EEA: considerations for public health response [Internet]. Stockholm, ECDC; 2024 [cited 2024 May 21]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/measles-eu-threat-assessment-brief-february-2024.pdf
3. Centers for Disease Control and Prevention (CDC). Stay alert for measles cases [Internet]. Atlanta, GA: CDC; 2024 [cited 2024 May 21]. Available from: https://emergency.cdc.gov/newsletters/coca/2024/012524.html
4. Public Health Agency of Canada. Statement from the Chief Public Health Officer of Canada on global increase in measles and risk to Canada [Internet]. Press release. Ottawa, ON: Government of Canada; 2024 Feb 23 [cited 2024 May 21]. Available from: https://www.canada.ca/en/public-health/news/2024/02/statement-from-the-chief-public-health-officer-of-canada-on-global-increase-in-measles-and-risk-to-canada.html
8. Image Source: Gupta SN, et al. J Family Med Prim Care. 2015;4(4):566 – 569; 2. Zmerli O, et al. Infect Prev Pract. 2021;3(1):100105; 3. Seto J, et al. Epidemiology and Infection. 2018;146:1707 – 1713; 4. UK Health Security Agency. National Measles Guidelines. Published February 2024. Available at: https://assets.publishing.service.gov.uk/media/65ddd0e9f1cab3001afc4774/national-measles-guidelines-Feb-2024.pdf (Accessed March 1, 2024).

Complications from Measles

- Complications from measles are more common in:[6,9]



1 in **4** people who get measles will need hospitalization[14]

- **Common complications from measles include:** otitis media, pneumonia, diarrhea
- **Severe complications can include:** spontaneous abortion, premature labour, low birth weight infants, encephalitis, death
- **Long-term sequelae can include:** permanent neurological sequelae, subacute sclerosing panencephalitis (SSPE)

8. Public Health Agency of Canada. Measles: for health professionals [Internet]. Ottawa, ON: Government of Canada; 2024 [Updated 2024 Feb 27; cited 2024 May 21] Available from: https://www.canada.ca/en/public-health/services/diseases/measles/health-professionals-measles.html
9. Centers for Disease Control and Prevention (CDC). Clinical overview of measles [Internet]. Atlanta, GA: CDC [cited 2024 May 21]. Available from: https://www.cdc.gov/measles/hcp/clinical-overview/?CDC_AAref_Val=https://www.cdc.gov/measles/hcp/index.html

Routine Measles Vaccination: Ontario's Publicly Funded Immunization Schedule[10]

Age	Number of Publicly Funded Doses	Ontario Publicly Funded Immunization Schedule[1,2]

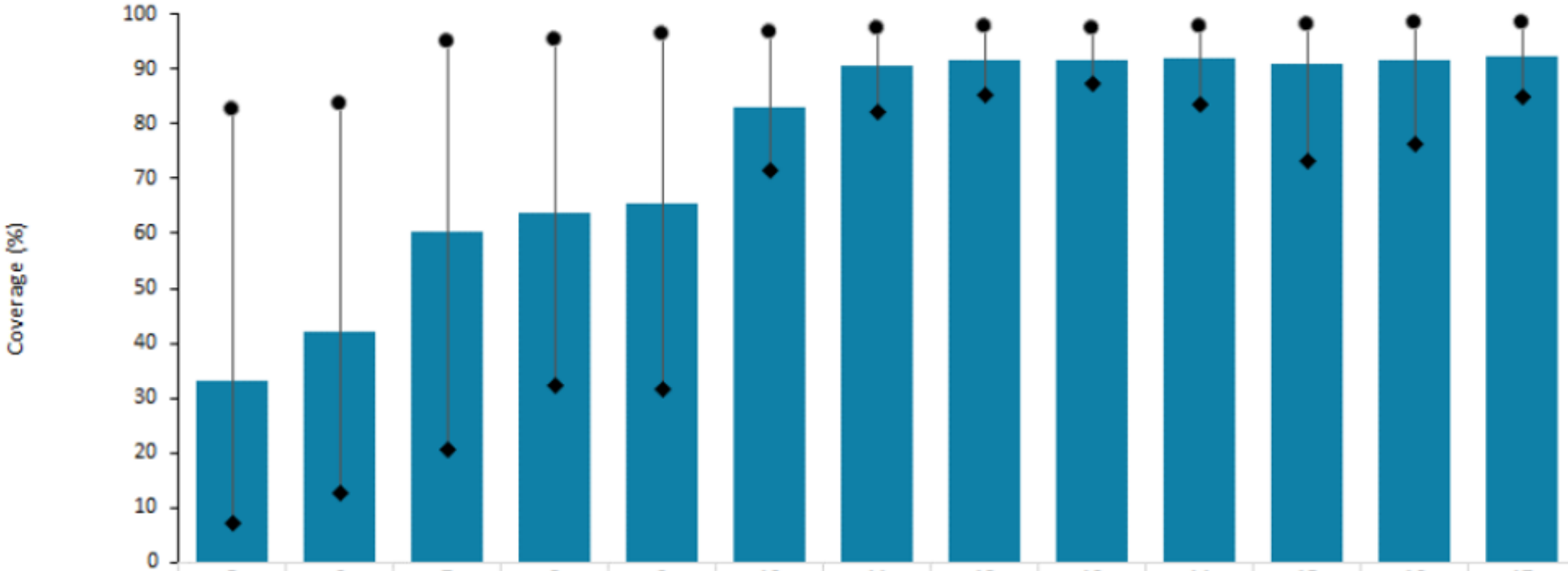
Children/adolescents 1 to 17 years	2 doses	• **Routinely given at:**
		  • 1 year of age (1st dose as MMR)
		  • 4 – 6 years of age (2nd dose as MMRV)

Adults 18 years and older	1 or 2 doses	• **Adults who have only received 1 dose of MMR are eligible to receive a 2nd dose:**
		  • Based on the healthcare provider's clinical judgement
		  • To healthcare workers
		  • To post-secondary students
		  • To individuals travelling to areas with increased measles transmission

- Many children may have missed routine immunizations due to the COVID-19 pandemic and these should be caught up urgently.

10. Ontario. Ministry of Health. Publicly funded immunization schedules for Ontario [Internet]. Toronto, ON: King's Printer for Ontario; 2022 [cited 2024 May 21]. Available from: https://www.ontario.ca/files/2024-01/moh-publicly-funded-immunization-schedule-en-2024-01-23.pdf

2-dose Measles Coverage From Immunizations Reported to Public Health Units Among 5 – 17-Year-Olds in Ontario (2022 – 23)[11]



	5	6	7	8	9	10	11	12	13	14	15	16	17
coverage	33.2	41.9	60.2	63.9	65.5	83.2	90.5	91.6	91.7	91.8	91.0	91.7	92.3
PHU minimum	7.1	12.5	20.6	32.2	31.7	71.5	82.3	85.3	87.4	83.7	73.2	76.2	85.0
PHU maximum	82.6	83.5	94.8	95.4	96.3	96.8	97.4	97.5	97.5	97.7	98.0	98.5	98.4

Immunization coverage based on doses reported to public health likely under-estimates the number of children protected.

11. Image source: Ontario Agency for Health Protection and Promotion (Public Health Ontario). Immunization coverage report for school pupils in Ontario: 2019-20 to 2022-23 school years [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [cited 2024 May 21]. Available from: https://www.publichealthontario.ca/-/media/Documents/I/24/immunization-coverage-2019-2023.pdf?rev=ca05fc8fc60549bca7ce2294e93994aa&sc_lang=en

Vaccination Recommendations Prior to Travel Outside of Canada[12]

Age Group	Canadian Immunization Guide Advice*	Notes
Infants (6 – 11 months)	1 dose of MMR vaccine	• 2 additional doses of measles-containing vaccine must be administered on or after 12 months of age to ensure long term protection
Children and adults aged ≥12 months and born in/after 1970	2 doses of measles-containing vaccine† (total)	• This includes an 'early' second dose of measles-containing vaccine†‡ for children < 4 years of age who have received the first dose
Adults born before 1970	1 dose of MMR vaccine (total)	• 1 dose unless there is lab evidence of immunity or history of lab-confirmed measles (vaccination is recommended over serological testing)

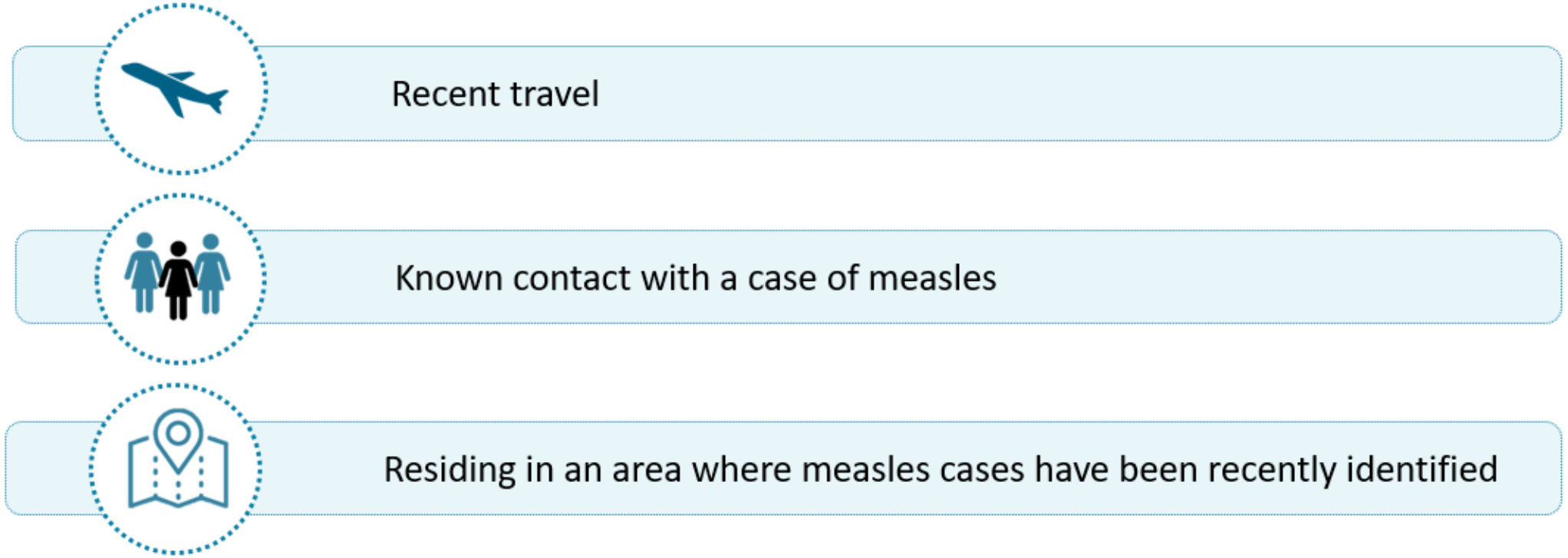
- MMR, measles, mumps and rubella vaccine.
- *Doses outlined are publicly funded in Ontario for travel to areas where disease is of concern. Refer to the Government of Canada's Travel Health Notices to Access Up To Date Information on Measles Outbreaks Occurring Outside of Canada
- † MMR or MMRV can be used (note: age indications for vaccine products differ)
- ‡ If a dose given for travel is administered on or after the first birthday and is separated from any previous live attenuated vaccine by at least 28 days, the dose is valid and will meet school-entry immunization requirements in Ontario.

12. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Measles: information for health care providers [Internet]. 2nd ed. Toronto, ON: King's Printer for Ontario; 2024 [cited 2024 May 21]. Available from: https://www.publichealthontario.ca/-/media/Documents/M/24/measles-information-health-care-providers.pdf?rev=b0bd7e50949344229d7dc3a4f866e413&sc_lang=en

Case and Contact Management

When to Suspect Measles[13]

Clinicians should consider measles in patients presenting with clinically compatible signs and symptoms, especially if they are unvaccinated, partially vaccinated, have unknown immunization status or are immunocompromised, and there is a potential exposure risk, including:



13. Public Health Ontario. At a Glance, Measles: Information for Health Care Providers (Draft 3rd Edition).

Management of Suspected Measles[13,14]

If you suspect measles infection in a patient:

1. Provide the patient with a medical mask (if able to tolerate use and no contraindications)
2. Promptly isolate the patient in a negative pressure room with the door closed, if available (if not available, place in a single patient room with the door closed)
3. Obtain specimens for testing
4. ***Contact your local public health unit immediately to report the suspect case (do not wait for laboratory confirmation) and to receive additional guidance***
5. Provide isolation guidance to the patient while results are pending

13. Public Health Ontario. At a Glance, Measles: Information for Health Care Providers (Draft 3rd Edition).
14. Ontario. Ministry of Health. Ontario public health standards: requirements for programs, services and accountability. Infectious disease protocol. Appendix 1: case definitions and disease-specific information [draft]. Toronto, ON: King's Printer for Ontario; 2024.

Common Questions

- What actions need to be taken if a measles case was communicable during air travel?
- What are the roles and responsibilities of various organizations?

Measles Cases Communicable During Air Travel[15,16]

If measles case was communicable on flight and it is within 21 days of the flight the following roles/actions apply:

Public Health Unit (PHU)	Public Health Ontario (PHO)	Public Health Agency of Canada (PHAC)
• Collects flight information and shares with PHO	• PHO communicates flight information to PHAC	• PHAC notifies relevant country/countries about measles exposures based on the flight itinerary
• Issues a media advisory that describes the flight(s), in addition to any other community exposure locations	• PHO emails with the airline(s) involved to advise of them of possible exposure for the purposes of flight crew notification	• PHAC provides PHO contact information for relevant airline(s)
• Posts a public health alert (CNPHI) alert to communicate the flight information to public health partners	• PHO coordinates with any other PT involved (i.e., domestic airline or if case resides outside of ON)	

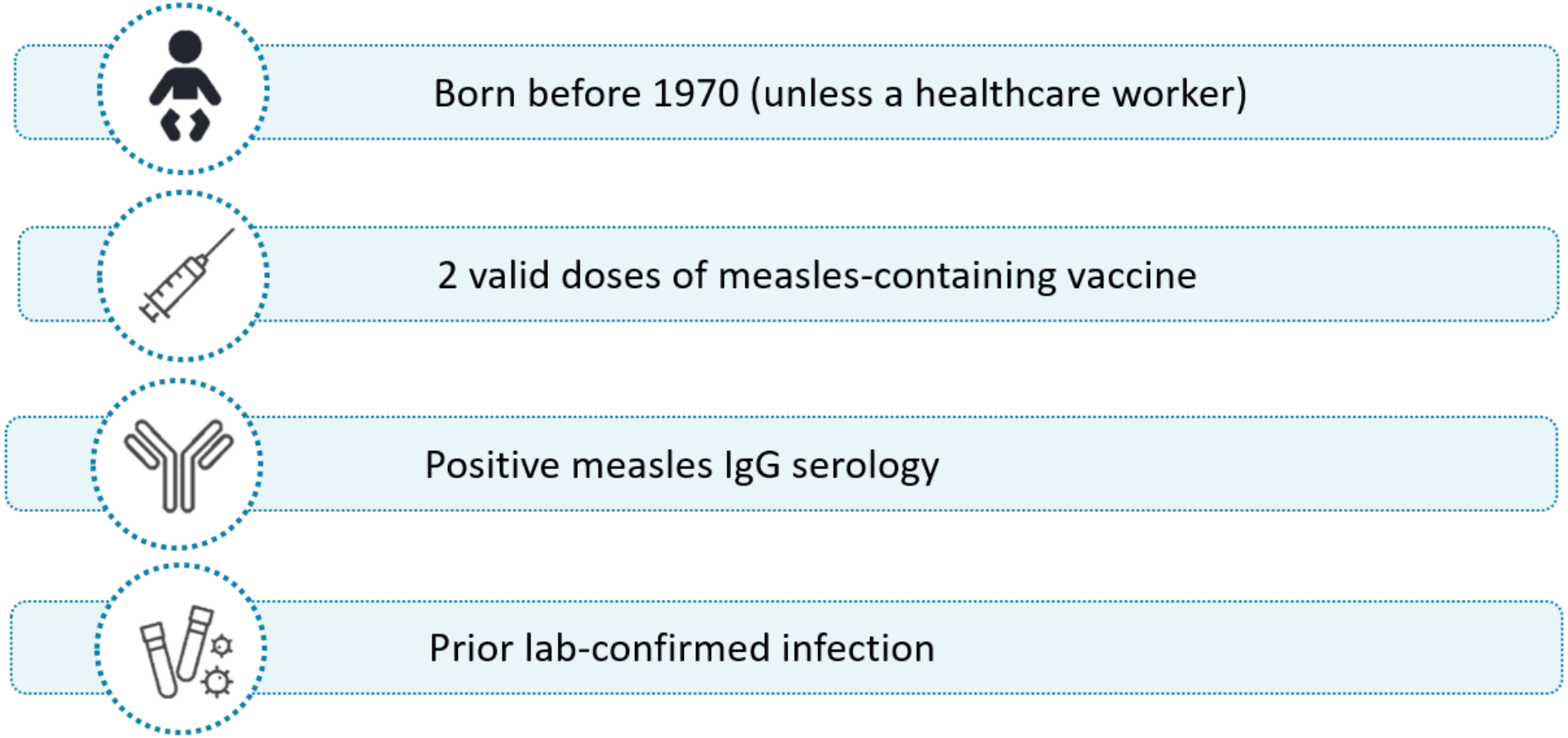
15. Public Health Agency of Canada, Communicable and Infectious Disease Steering Committee. Process for contact management for measles cases communicable during air travel (Interim Guidance). Ottawa, ON: Government of Canada; 2024.
16. CNPHI, Canadian Network for Public Health Intelligence; ON, Ontario; PHAC, Public Health Agency of Canada; PHO, Public Health Ontario. Communicable and Infectious Disease Steering Committee, Public Health Agency of Canada. Process for Contact Management for Measles Cases Communicable During Air Travel (Interim Guidance). Released May 2024.

Common Questions

- What is the definition of measles susceptibility for measles contact management?
- What are the options available for post-exposure prophylaxis (PEP)?

Ontario Presumptive Immunity Criteria for Contact Management[17]

Measles contacts are considered susceptible unless they meet at least one of the following:



17. Ontario. Ministry of Health. Ontario public health standards: requirements for programs, services and accountability. Infectious disease protocol. Appendix 1: case definitions and disease-specific information [draft]. Toronto, ON: King's Printer for Ontario; 2024

Rationale for Measles Post-exposure Prophylaxis[17]

- MMR vaccine, if given within **72 hours of first exposure**, can reduce the risk of measles infection
- Immunoglobulin (Ig), administered either intramuscularly (IMIg) or intravenously (IVIg) **within 6 days of exposure**, may also reduce the risk of infection, but the primary rationale is to **reduce clinical severity**, if measles infection develops

17. Ontario. Ministry of Health. Ontario public health standards: requirements for programs, services and accountability. Infectious disease protocol. Appendix 1: case definitions and disease-specific information [draft]. Toronto, ON: King's Printer for Ontario; 2024.

Ontario: 2024 Guidance on Measles PEP for Susceptible Contacts[17,18]

Population	Time Since Exposure: ≤72 hours	Time Since Exposure: 73 hours – 6 days
Susceptible infants <6 months of age	IMIg (0.5 mL/kg)[a,b]	IMIg (0.5 mL/kg)[a,b]
Susceptible immunocompetent infants 6 – 11 months of age	MMR vaccine[a]	IMIg (0.5 mL/kg)[b]
Susceptible immunocompetent individuals ≥12 months of age	MMR vaccine	MMR vaccine for long-term protection (not PEP)[c]
Susceptible pregnant individuals[d]	IVIg (400 mg/kg) or IMIg (0.5 mL/kg, limited protection if bodyweight ≥30 kg)[e]	IVIg (400 mg/kg) or IMIg (0.5 mL/kg, limited protection if bodyweight ≥30 kg)[e]
Susceptible immunocompromised individuals ≥6 months of age[f]	IVIg (400 mg/kg) or IMIg (0.5 mL/kg, limited protection if bodyweight ≥30 kg)[e]	IVIg (400 mg/kg) or IMIg (0.5 mL/kg, limited protection if bodyweight ≥30 kg)[e]

[a] Two doses of measles-containing vaccine are still required after the first birthday for long-term protection;
[b] If injection volume is a concern, IVIg (400 mg/kg) may be considered;
[c] MMR vaccine will not be effective PEP if given >72 hours after exposure; however, starting and completing a two-dose series should not be delayed and will provide long-term protection;
[d] The 2018 NACI guidance on IVIg as PEP used the Canadian Immunization Guide definition of immunity of at least 1 dose of measles-containing vaccine for adults born on or after 1970. Therefore, recommendations for PEP using IVIg for adults, should consider the intensity and duration of the measles exposure, and the immunization status (0 vs. 1 dose) of the contact. Serology may also play a role in supporting decisions for IVIg, if it can be obtained in a timely fashion. MMR vaccine should be provided postpartum, as needed, to provide long-term protection;
[e] For individuals weighing 30 kg or more, IMIg will not provide complete protection but may provide partial protection
[f] Please refer to the additional considerations outlined in the "Host Susceptibility and Resistance" section for further information regarding assessing the susceptibility of immunocompromised individuals.
IMIg, intramuscular immunoglobulin; IVIg, intravenous immunoglobulin; MMR, measles, mumps, rubella; NACI, National Advisory Committee on Immunization; PEP, post-exposure prophylaxis.

17. Ontario. Ministry of Health. Ontario public health standards: requirements for programs, services and accountability. Infectious disease protocol. Appendix 1: case definitions and disease-specific information [draft]. Toronto, ON: King's Printer for Ontario; 2024.
18. Ontario. Ministry of Health. Ontario public health standards: requirements for programs, services and accountability. Infectious disease protocol. Appendix 1: case definitions and disease-specific information. Disease: measles. Effective: March 2024 [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [cited 2024 May 21]. Available from: https://www.ontario.ca/files/2024-03/moh-measles-appendix-en-2024-03-19.pdf

Exclusion of Susceptible Contacts

- Ontario appendix provides direction for high risk settings (i.e. schools, daycares, healthcare settings) and identifies the importance of professional judgement ("at the discretion of the Medical Officer of Health") for other settings
- Period of exclusion: 5th day after the first exposure to the 21st day after the last exposure

Exclusion of Susceptible Contacts Who Are Not Healthcare Workers[18]

Measles vaccination status	Contacts who attend high risk settings (school, daycare)	Notes
Unknown Unvaccinated (0 doses)	Exclusion if vaccine as PEP not received within 72 hours*	• Serology may play a role in guiding exclusion decisions for those with unknown vaccine history
1 dose	In general, exclusion until 2nd dose of vaccine is received (can immediately return to school/daycare after dose is received)	• Serology may be helpful for close (e.g. household) contacts • Recognizes effectiveness (85-95%) for 1 dose of vaccine • Offering a 2nd dose improves protection against any secondary cases that may arise

* Susceptible contacts who receive who receive IMIg/IVIg as PEP should also be considered for exclusion from high-risk settings (e.g., health care settings, childcare and school settings) at the discretion of the medical officer of health

17. Ministry of Health. Ontario Public Health Standards Infectious Disease Protocol Appendix 1: Case Definitions and Disease-Specific Information, Disease: Measles. Published 2024

18. Ontario. Ministry of Health. Ontario public health standards: requirements for programs, services and accountability. Infectious disease protocol. Appendix 1: case definitions and disease-specific information. Disease: measles. Effective: March 2024 [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [cited 2024 May 21]. Available from: https://www.ontario.ca/files/2024-03/moh-measles-appendix-en-2024-03-19.pdf

Acknowledgements

- Janice Sarmiento
- Members of IVPD team at Public Health Ontario
- Local Public Health Units and other health system partners in Ontario

Measles Laboratory Diagnosis at PHO

Measles Laboratory Diagnosis (1/2)

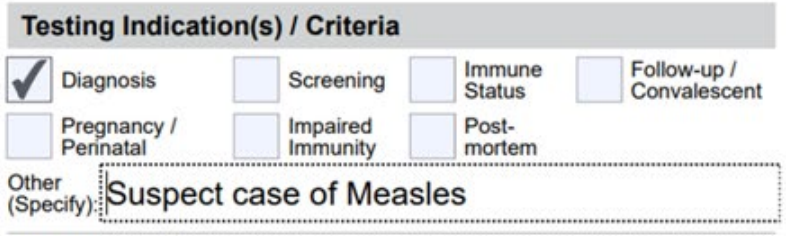
- Important as rash can be confused with other viral exanthemous illness.
- Milder forms can occur in previously vaccinated.
- low prevalence setting like Canada, all cases need to be lab-confirmed
- Lab confirmation:
  - Detection of measles virus RNA using a Nucleic Acid Amplification Test (NAAT) (i.e., PCR) from an appropriate clinical specimen.
  - Measles IgM antibody in single serum sample during acute phase can be diagnostic in persons with epidemiological link to a lab confirmed case **OR** recently travelled to an area of known measles activity.
  - Measles IgG seroconversion by any standard serologic assay between acute and convalescent sera.

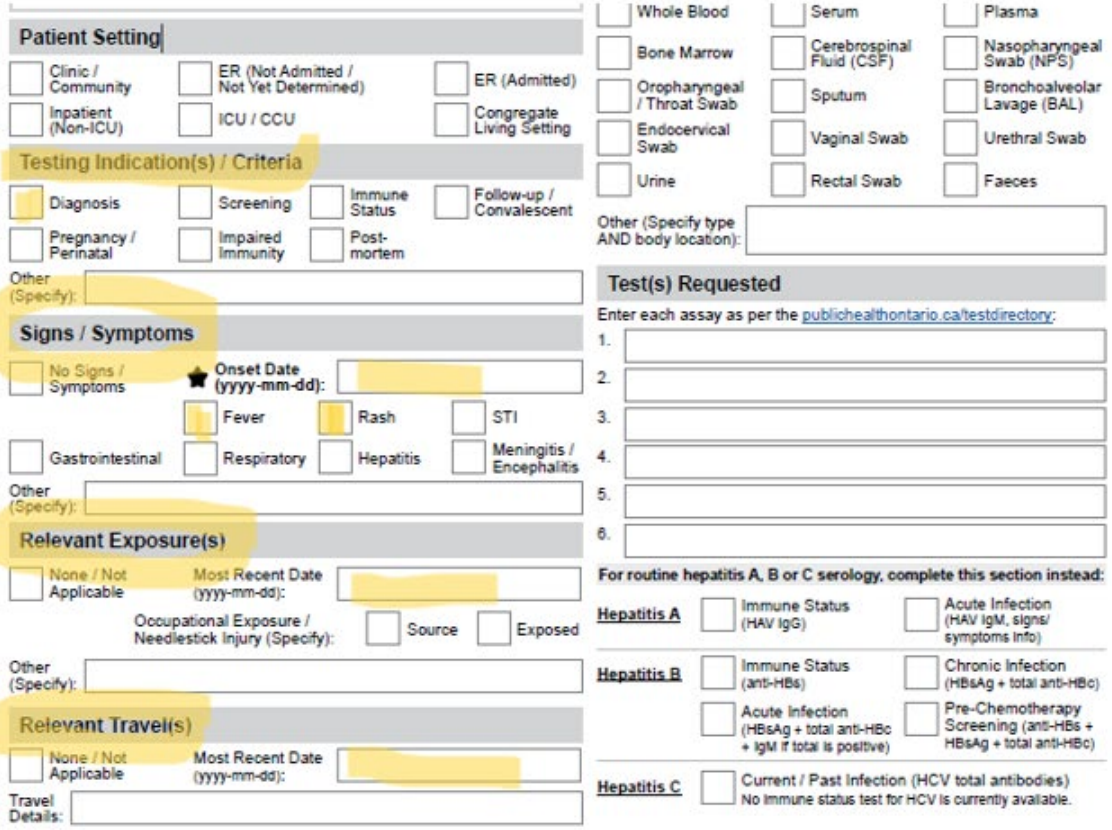
Measles Laboratory Diagnosis (2/2)

- For suspected cases of Measles
- Measles PCR is a diagnostic test for the detection of viral RNA in clinical specimens
- Useful during the early phase of the disease following symptom onset.
- For diagnosis of symptomatic patients, collect NP and/or throat, as well as urine specimens **and** blood for serology
- Nasopharyngeal swab or aspirate and/or a throat swab should be collected within 7 days of rash onset. Use non-expired collection media
- Urine should be collected within 14 days of rash onset and submitted in a sterile container. CTNG specimen container will be rejected for testing

Request for Testing

Clearly mark “Suspect case of measles” in the Testing Indications section of the laboratory requisition for both virus detection (PCR) and diagnostic serology.





Temporary Guidance for Prioritized Measles Testing

To help PHO's laboratory **prioritize measles** requests:

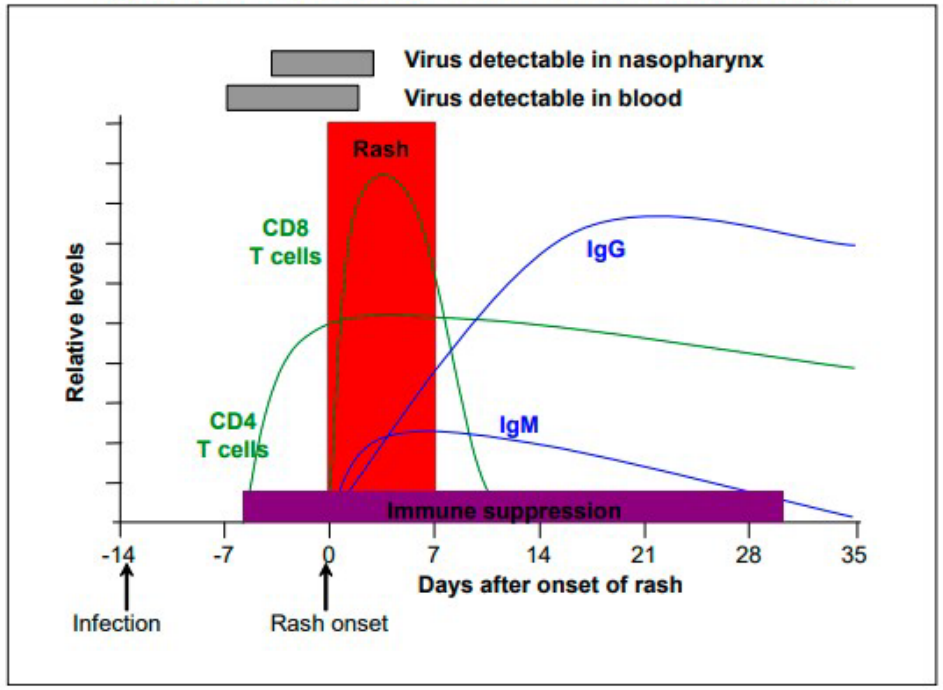
- STAT measles specimens must be shipped **separate** from routine specimens
- Clearly mark the outside of the package/shipping bag '**STAT**'
- Notify the lab when the specimens are ready to be shipped
  - During regular hours, call PHO's Laboratory Customer Service Centre: 416-235-6556, or Toll Free: 1-877-604-4567
  - During after-hours, call the Duty Officer: 416-605-3113

- Send the package **directly** to PHO's laboratory
  - PHO's laboratory sites in Toronto, Kingston, Timmins, Ottawa, Hamilton, and Thunder Bay offer measles PCR testing
  - Refer to the Measles PCR Test Information Sheet for further information including turnaround time and test frequency

Measles – Serology (1/2)

- Measles has one serotype
- Measles IgG testing will be performed on **all** requests for Measles immunity serology.
- Measles IgG & IgM testing will be performed on diagnostic requests **only** when clinical information is provided on the General Test Requisition Form.
- **Convalescent Specimen:** Collect the specimen a minimum of 7 and up to 30 days after the acute specimen collection.

Figure 3. Immune responses in acute measles infection (after [7])



19. Image source: European Centre for Disease Prevention and Control (ECDC). Eurosurveillance - Volume 29, Issue 7, 15 February 2024 [Internet]. Stockholm: ECDC; 2024 [cited 2024 May 21]. Available from: https://www.eurosurveillance.org/content/eurosurveillance/29/7

Measles - Serology (2/2)

- Measles IgM antibody in single serum sample during acute phase **can be** diagnostic.
- If prevalence very low, most positive IgM will be false positive.
- **IgM DETECTION:** The day the rash develops up to 4 to 5 weeks.
- Capture IgM positive in 77% of those collected within 72hr of rash onset, 100% collected 4-11d after onset rash.

When to expect IgM Reactive

- Get IgM response following vaccination or infection
- IgM response absent on revaccinating those previously immunized
- IgM response may follow clinical infection independent of prior immunization status

Measles RT-PCR - Test Methods

- Measles PCR test is a real-time RT-PCR assay
- PHO uses a laboratory developed test targeting sequences in the measles virus nucleoprotein (N3), fusion (F1) and hemagglutinin (H1) genes
- It is only performed at PHO in Ontario
- Positive measles PCR will be tested first in-house with measles vaccine genotype PCR, all negative in-house measles vaccine genotype PCR will be referred to NML for full genotyping

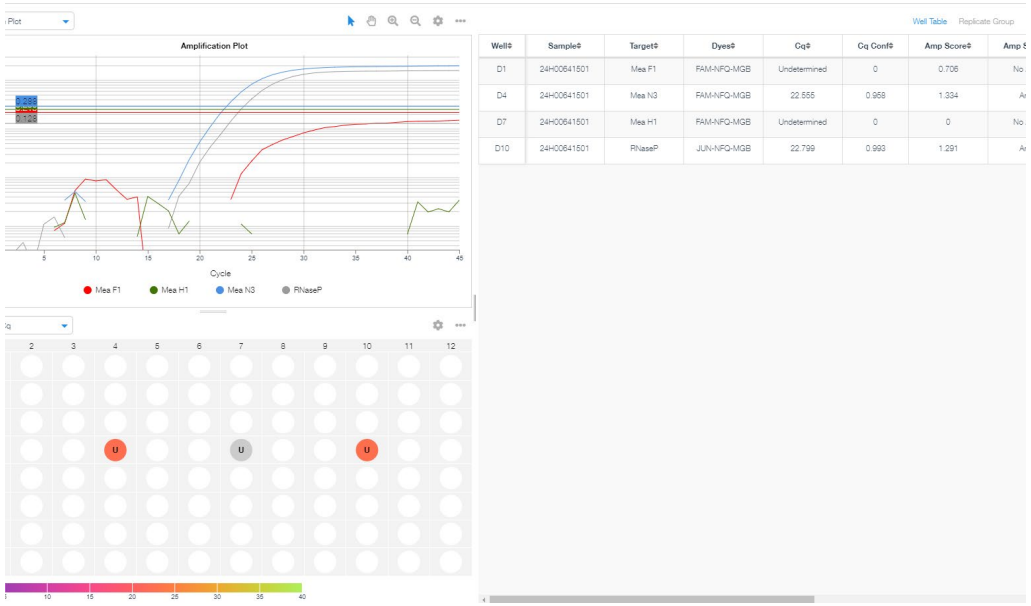
Measles RT-PCR - Test Methods (cont'd)

- RT-PCR – preferred in low prevalence setting where many false -positive IgM
- Helpful if measles vaccine given as part of outbreak response (IgM won't help) or in settings of high vaccine coverage

Recent Studies[20]

A recent study reported out of Switzerland, and also in a letter to the editor from Italy, details the findings of recently detected (late 2021) measles genotype D8 strains that have 3 nucleotide mismatches, which appears to have resulted in a slight loss of analytical sensitivity.

NML did confirm a reduction in assay analytical sensitivity in one target (in this case the N gene) is not expected to impact the ability to detect measles cases (clinical sensitivity).



20. Image source: European Centre for Disease Prevention and Control (ECDC). Eurosurveillance - Volume 29, Issue 7, 15 February 2024 [Internet]. Stockholm: ECDC; 2024 [cited 2024 May 21]. Available from: https://www.eurosurveillance.org/content/eurosurveillance/29/7

Measles RT-PCR - Assay Sensitivity and Specimen Types[21]

- Literature review indicates an overall sensitivity range of 95.5% to 100% confidence level among NP (95.5%), Throat (100%) and Urine (96.7%) specimens for detection of measles.
- Sensitivity of the assay is relative to the onset of symptoms and in relation to collection time.

TABLE II. Sensitivity of Various Measles Diagnostic Tests With Different Specimen Types

Days after rash onset	Serum		NPA		TS/TNS		Urine	
	IgM	RT-PCR	Culture	RT-PCR	Culture	RT-PCR	Culture	RT-PCR
<0–3	91.2% (82.9–95.9%) n = 91	81.0% (70.6–88.4%) n = 84	82.2% (67.4–91.5%) n = 45	93.5% (77.2–98.9%) n = 31	63.0% (42.5–79.9%) n = 27	100% (82.2–99.6%) n = 23	66.7% (43.1–84.5%) n = 21	94.1% (69.2–99.7%) n = 17
4–7	98.5% (90.7–99.9%) n = 66	77.8% (64.1–87.5%) n = 54	73.7% (48.6–89.9%) n = 19	100% (71.7–99.3%) n = 13	40.0% (23.2–59.3%) n = 30	100% (81.5–99.6%) n = 22	50.0% (25.5–74.5%) n = 16	100% (67.9–99.2%) n = 11
>7	100% (86.7–99.7%) n = 32	50.0% (26.8–73.2%) n = 18	NA	NA	0% (1.5–48.3%) n = 6	100% (51.7–98.5%) n = 6	0% (4.9–80.2%) n = 2	100% (19.8–95.1%) n = 2
Overall	95.2% (90.9–97.7%) n = 189	76.3% (68.7–82.6%) n = 156	79.7% (67.4–88.3%) n = 64	95.5% (83.3–99.2%) n = 44	46.0% (33.6–59.0%) n = 63	100% (91.3–99.8%) n = 51	56.4% (39.8–71.8%) n = 39	96.7% (80.9–99.8%) n = 30

Equivocal result was regarded as positive when calculating sensitivity of detection of anti-measles IgM by ELISA; numbers in brackets represent 95% confidence interval.
NA, not available; n, number of samples tested.

21. Source: Gibson SK, Wong AH, Lee WY, Lau CS, Cheng PKC, Leung PCK, et al. Comparison of laboratory diagnostic methods for measles infection and identification of measles virus genotypes in Hong Kong. J Med Virol. 2010;82(10):1773-81. Available from: https://doi.org/10.1002/jmv.21888

Measles RT-PCR - PHO Retrospective Analysis

Table 2: Measles PCR results 165 individuals confirmed lab measles by PCR for throat, nasopharyngeal, and urine specimen sources, PHO, January 1, 2014 to March 20, 2024

Specimen source	Measles PCR results		
	Detected	Tested	Percent detected
Throat	28	30	93.3%
Urine	116	126	92.1%
Nasopharyngeal	108	118	91.5%

Data based on 307 specimens tested from 165 individuals

Measles RT-PCR - PHO Retrospective Analysis - Data Caveats

- Results should be interpreted with caution due to limited sample size, particularly for throat specimens (n=30)
- Lack of information about disease onset in relation with specimen collection
- This may impact test performance for specimen types, particularly if a specimen was collected too early or too late during the course of disease

Table 3 - Measles PCR percent detected for urine, nasopharyngeal, and throat specimen sources from lab confirmed individuals submitting dual or triple specimens, PHO, January 1, 2014 to March 20, 2024

Specimen source combination	Percent detected		
	Urine	Nasopharyngeal	Throat
Urine and nasopharyngeal	90.9%	88.6%	NA
Throat and nasopharyngeal	NA	81.8%	90.9%
Throat and urine	92.0%	NA	96.0%
Throat, nasopharyngeal and urine	100%	80.0%	90.0%

Results of urine, nasopharyngeal and throat specimen sources were compared within the same individual

Genotyping

- Positive measles PCR will be tested first in-house with measles vaccine genotype PCR. Vaccine strain is genotype A
  - Thirteen individuals were positive for the measles vaccine strain in 2024
- All PCR-positive specimens (vaccine strain PCR negatives, wild-type MeVs) forwarded to NML for genotyping
- Allows epidemiological tracking of viruses globally
- Genotyping done by sequence of a small fragment (3%) of the genome, the N gene - 450 nucleotides

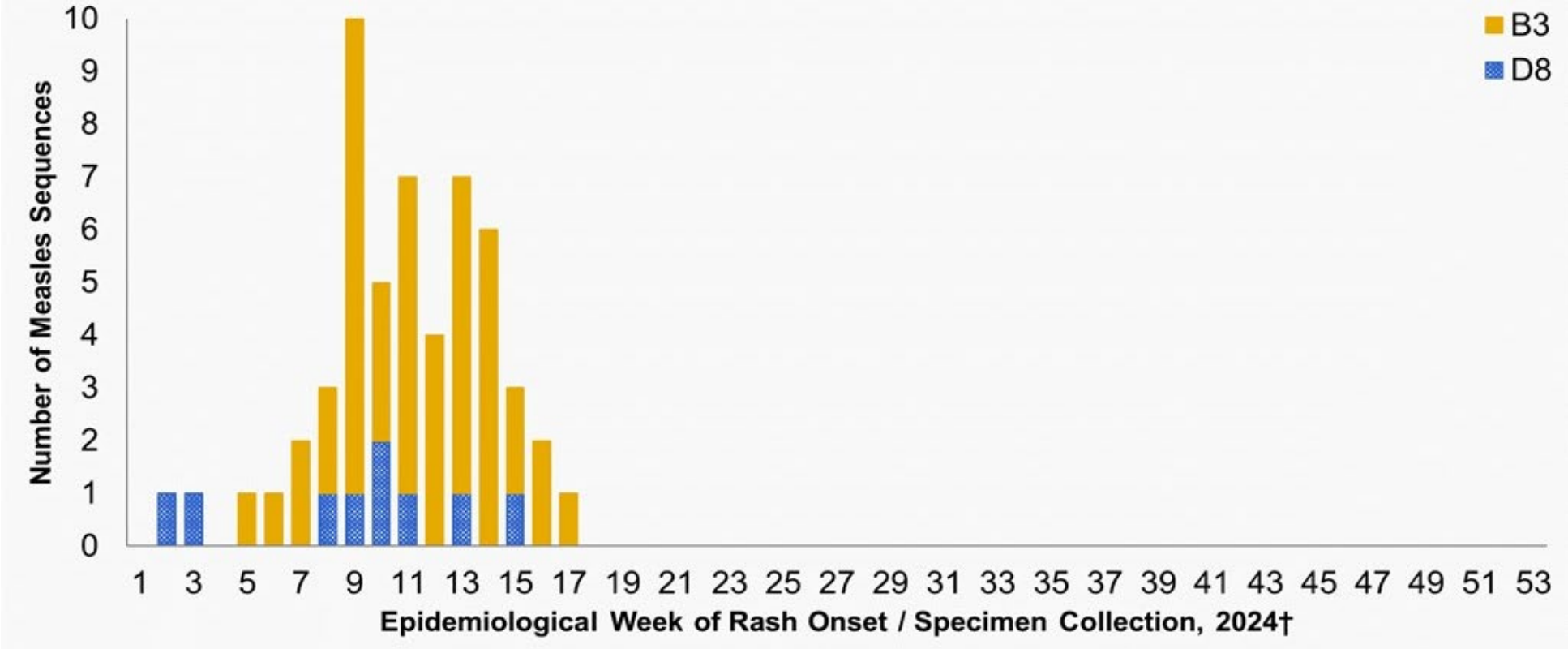
Measles Virus Genotypes

- The WHO Global Measles and Rubella Laboratory Network (GMRLN) established standard methods for analysing the genetic characteristics of wild-type MeVs
- 24 genotypes represented the genetic diversity of MeV over time, 18 are now considered inactive, as they have not been detected in at least 10 years
- Of the 6 genotypes currently defined as active:
  - Five genotypes, **D8, B3, D9, H1 and D4**, were reported in 2019
  - Three genotypes, **D8, B3 and D4,** in 2020
  - And only 2, **B3 and D8**, in 2021
- Between 2018 and 2021, 97% of the sequences reported to Measles Nucleotide Surveillance were genotype D8 (67%) or genotype B3 (30%)

WEEKLY EPIDEMIOLOGICAL RECORD, NO 39, 30 SEPTEMBER 2022

Distribution of Measles Genotypes Detected in 2024 – PHAC[22]

Measles PHAC Weekly Monitoring Report – Week 17: April 21 to April 27, 2024
Number of cases of measles (n=69)



22. Image source: Public Health Agency of Canada. Measles & Rubella Weekly Monitoring Report – Week 17: April 21 to April 27, 2024 [Internet]. Ottawa, ON: Government of Canada; 2024 [cited 2024 May 21]. Available from: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/measles-rubella-surveillance/2024/week-17.html

Measles Genotypes of Strains Circulating in Ontario

- Both D8 and B3 strains were evenly identified from Measles genotype among 12 individuals tested at PHO Laboratory January 1, 2024 to May 11, 2024
- Data includes only successful genotype results from NML
- Genotyping reports needs to be interpreted in the context of epi history, time, global circulation of the strain, similarity to other relevant strains, etc.

Important Pearls

- Prioritize measles requests
- RT-PCR – preferred in low prevalence setting where many false-positive IgM
- For diagnosis of symptomatic patients, collect NP and/or throat, as well as urine specimens for molecular assay **and** blood for serology
- Nasopharyngeal swab or aspirate and/or a throat swab should be collected within 7 days of rash onset. Use non-expired collection media
- Immunization with Measles-containing vaccine is preferred, rather than ordering serology to determine immune status

Acknowledgements

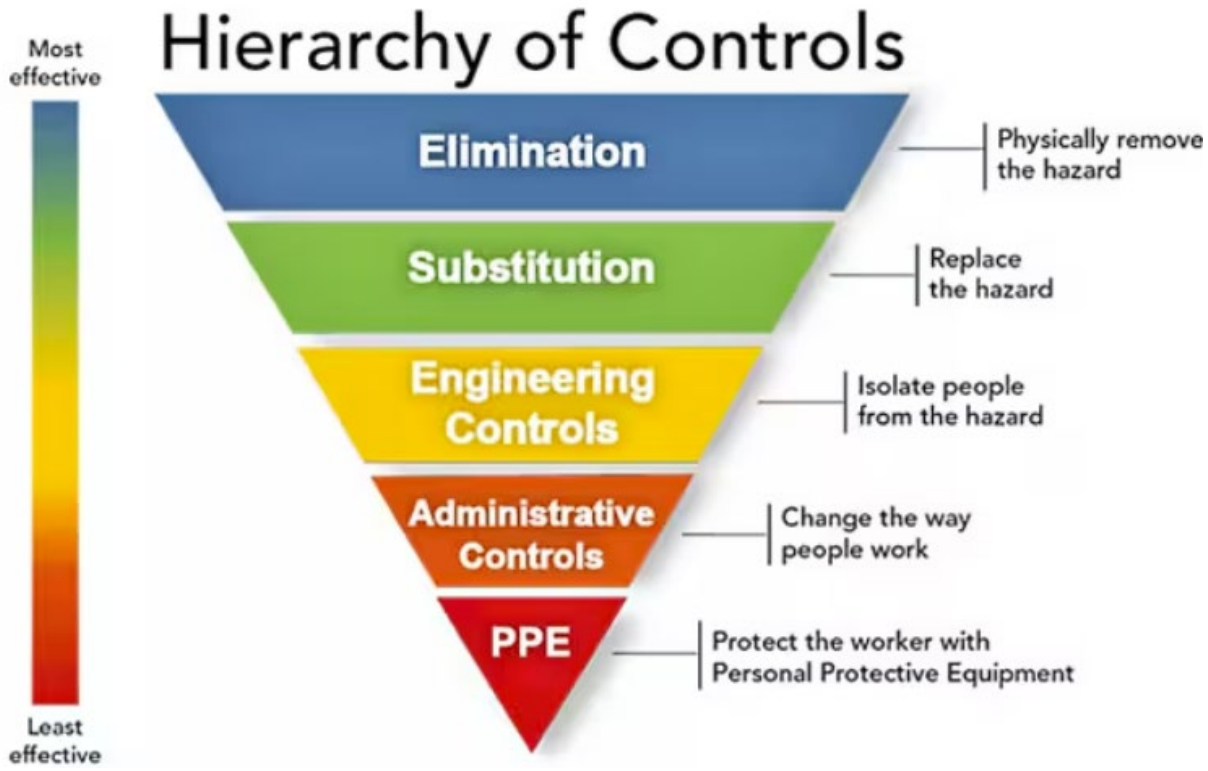
- PHO virus detection lab
- PHO Preventable diseases lab
- Regional labs
- PHO IORT
- PHO LSDM
- National Microbiology Laboratory

Measles IPAC update for Health Care Workers and Health Care Settings

Hierarchy of Controls[23]

As relates to measles:

- Elimination of infection
- Airborne Infection Isolation room (AIIR)
- Organizational risk assessment; pre-placement vaccination/ serology; post-exposure management including work restrictions
- PPE



23. Image source: Centers for Disease Control and Prevention (CDC). About hierarchy of controls [Internet]. Atlanta, GA: CDC; 2024 [cited 2024 May 22]. Available from: https://www.cdc.gov/niosh/hierarchy-of-controls/about/?CDC_AAref_Val=https://www.cdc.gov/niosh/topics/hierarchy/default.html

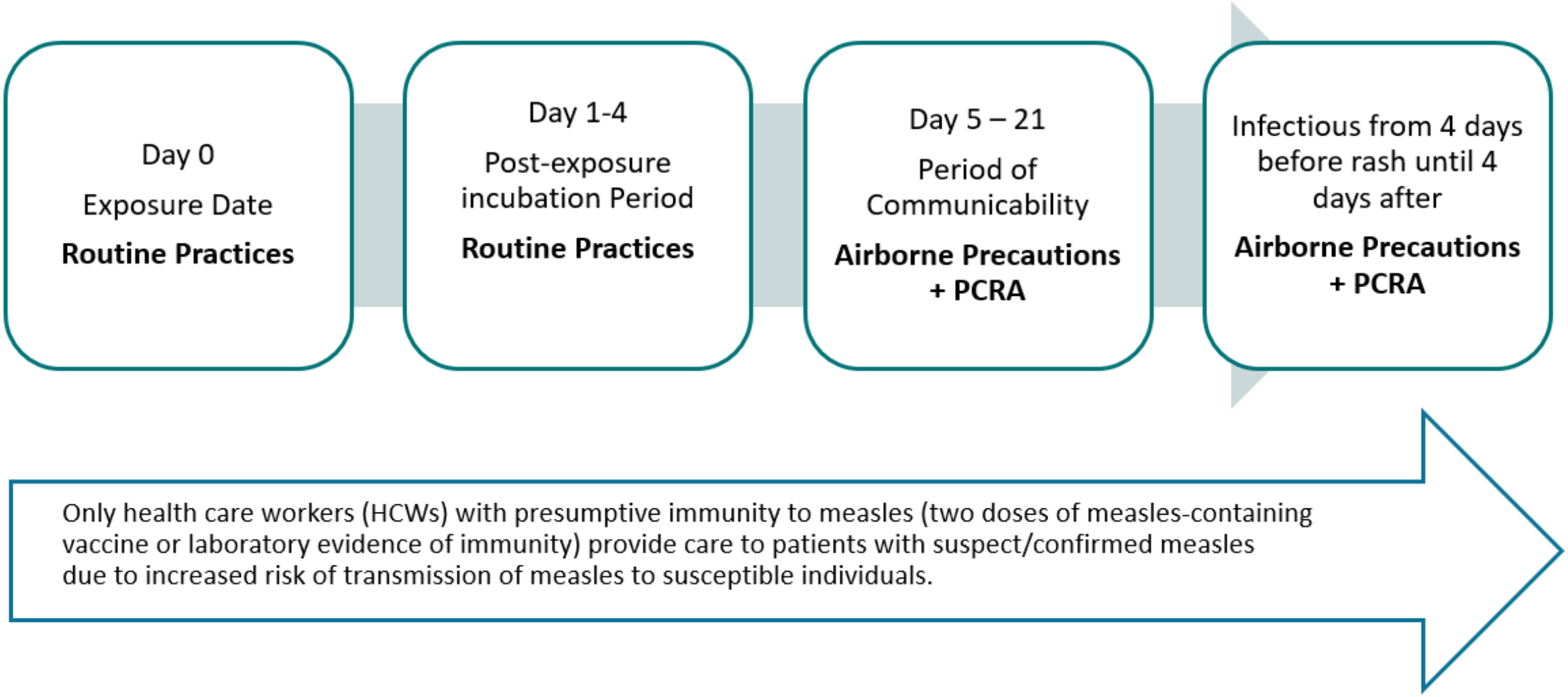
Example of Organizational Risk Assessment (ORA)

- Settings at risk:
  - Hospital ER/Urgent Care/Paediatric clinics
  - Public health PEP and vaccine catch-up clinics
  - Primary care
  - Specimen Collection Centres
- Patients at risk:
  - Pregnant, children less than five, immunocompromised
- Intersection of these groups—waiting rooms
- Mitigating factors:
  - Advance notification
  - Separate entrance/exit, bypassing waiting room and public spaces including washroom, cafeteria

ORA for Clinic Settings

- Evaluate potential for exposure to and/or transmission of measles at the clinic
- Determine the consequences of exposure to measles, considering transmission to HCWs and those attending the clinic
- Assess available control measures to mitigate exposure to or transmission of measles in the clinic
  - Assessment should include infrastructure of the clinic space (e.g., number of exam rooms, waiting spaces)
  - Immunization status of clinic workers
  - Education of clinic staff on the selection and use of PPE, including respirator fit-testing and accessibility of PPE

Measles Exposure Timeline



IPAC Practices for Patient Management

- Individuals with measles are considered infectious from 4 days prior to rash onset through to 4 days after rash onset
- A patient suspected of having a measles infection should be managed under **Routine Practices and Airborne Precautions** and **any additional PPE based on a PCRA** (e.g., gown, gloves, eye protection)
  - Schedule the patient visit to minimize exposure of others (e.g., at the end of the day)
  - Ensure the patient arrives wearing a well-fitted medical mask or promptly provide one
  - Immediately place the patient in an airborne infection isolation room (AIIR) with the door closed
  - If this is not available, the patient should be placed in a single room with the door closed. Room to remain closed and unavailable for 2 hours following patient visit

Measles Post-Exposure Prophylaxis/Vaccination/Primary Care Clinics and Specimen Collection Centres

- Clinics where individuals could be in their period of communicability should be scheduled separately from other clinics to avoid possible exposure
- Appointments should be booked as single consecutive appointments, excepting families who are assessed together as they are likely to have had similar exposures
- For PEP clinic, If confident patient is within 4 day window post-exposure and asymptomatic, patient is not required to wear a medical mask and HCWs can provide care following Routine Practices
  - Note: MMR given as PEP is within 72 hours of exposure; after 72 hours is considered vaccination update to provide protection for future exposure
  - Immune globulin to be given within 6 days of exposure (IV in hospital setting); Airborne Precautions to be implemented from Day 5

Measles Immunization for Health Care Workers

- Immunization status should routinely be determined at time of hire by vaccination records or serology (measles IgG)
- If immunization records unavailable, immunization with MMR preferable to ordering serology to determine immune status. No harm in giving MMR to an individual who is already immune
- Individuals travelling outside of Canada should ensure they are adequately protected prior to travelling: Measles Vaccines: Canadian Immunization Guide - Canada.ca[28]

24. Government of Canada. Measles vaccines: Canadian Immunization Guide [Internet]. Ottawa, ON: Government of Canada; 2020 [updated 2020 Sep; cited 2024 May 21]. Part 4, Immunizing agents. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-12-measles-vaccine.html

Occupational Risk of Measles in HCWs

- HCW risk of measles is higher than the general population
- HCWs are at increased risk for occupationally acquired measles infection, in part due to increased exposure to patients who are ill with measles seeking health care
- Patients who are ill enough to be hospitalized are also generally at the peak of their communicability with high viremia and viral shedding

IPAC Considerations and PPE for HCWs Providing Care to Patients with Suspect/Confirmed Measles[25]

- All health care workers (HCWs) need documented immunity to measles (2 doses of MMR or history of laboratory-confirmed infection or serological evidence of immunity, **regardless of year of birth**
- Only HCWs with presumptive immunity should provide care or be in the room with patients with suspect/confirmed measles
- Recent scientific literature describes measles transmission and associated outbreaks in hospitals in both susceptible HCWs and in HCWs with presumptive immunity
- **All HCWs should wear a fit-tested, seal-checked N95 respirator when entering the room and/or caring for a patient with suspect/confirmed measles**

25. Ontario Hospital Association; Ontario Medical Association. Measles surveillance protocol for Ontario hospitals. Toronto, ON: Ontario Hospital Association; 2019

Point-of-Care Risk Assessment (PCRA)[26]

- An evaluation of the interaction of the health care provider, the patient/client and the patient/client's environment to assess and analyze the potential for exposure to infectious disease
- The risk assessment process is dynamic, based on continuing changes in information as care progresses, thus must be done before each interaction with a client/patient/resident
- Informs the placement of the patient and the selection of personal protective equipment (PPE)

26. Ontario Agency for Health Protection and Promotion (Public Health Ontario), Provincial Infectious Diseases Advisory Committee. Routine practices and additional precautions in all health care settings [Internet]. 3rd ed. Toronto, ON: Queen's Printer for Ontario; 2012 [cited 2024 May 21]. Available from: https://www.publichealthontario.ca/-/media/documents/b/2012/bp-rpap-healthcare-settings.pdf?la=en

Global Technical Consultation Report on Proposed Terminology for Pathogens that Transmit through the Air (WHO, April 2024)

- Individuals infected with a respiratory pathogen can generate and expel infectious particles containing the pathogen through their mouth or nose by breathing, talking, singing, spitting, coughing or sneezing. These particles should be described with the term infectious respiratory particles or IRPs
- Particles exist on a continuum of sizes and no single cut off points should be applied…facilitates moving away from dichotomy of terms –aerosols (smaller) and droplets (larger) particles
- Starting point for IPAC review and discussion of any proposed changes in terminology or practice

27. World Health Organization (WHO). Global technical consultation report on proposed terminology for pathogens that transmit through the air [Internet]. Geneva: WHO; 2024 [cited 2024 May 21]. Available from: https://cdn.who.int/media/docs/default-source/documents/emergencies/global-technical-consultation-report-on-proposed-terminology-for-pathogens-that-transmit-through-the-air.pdf?sfvrsn=de07eb5f_1&download=true

‘Transmission Through the Air’[27]

- **‘Airborne transmission/inhalation’** occurs when IRPs are expelled into the air and enter the respiratory tract of another person and may potentially cause infection
- Can occur over short or long distances
  - Distance traveled depends on particle size, mode of expulsion and environmental conditions such as airflow, humidity, temperature, ventilation and setting
- Portal of entry of an IRP with respiratory tract tissue during airborne transmission can theoretically occur at any point along the human respiratory tract, but preferred sites of entry may be pathogen specific.

27. World Health Organization (WHO). Global technical consultation report on proposed terminology for pathogens that transmit through the air [Internet]. Geneva: WHO; 2024 [cited 2024 May 21]. Available from: https://cdn.who.int/media/docs/default-source/documents/emergencies/global-technical-consultation-report-on-proposed-terminology-for-pathogens-that-transmit-through-the-air.pdf?sfvrsn=de07eb5f_1&download=true

Potential Modes of Transmission of IRPs[27]

Figure 1. Potential modes of transmission of infectious respiratory particles

Source: Developed by A. Manna and L. Bourouiba, adapted from (*8, 12, 22, 23*).

27. World Health Organization (WHO). Global technical consultation report on proposed terminology for pathogens that transmit through the air [Internet]. Geneva: WHO; 2024 [cited 2024 May 21]. Available from: https://cdn.who.int/media/docs/default-source/documents/emergencies/global-technical-consultation-report-on-proposed-terminology-for-pathogens-that-transmit-through-the-air.pdf?sfvrsn=de07eb5f_1&download=true

Cleaning Considerations

- Rooms, where Airborne Precautions have been initiated, are to be routinely cleaned and disinfected using a low-level disinfectant that has a drug identification number
- Environmental service workers should wear a fit-tested, seal-checked N95 respirator when in the room. Additional personal protective equipment (PPE) such as gloves, gown and eye protection are added based on PCRA
- The door must be kept closed to maintain negative pressure even if the patient is not in the room
- Note all PPE, including the respirator, **should be removed after exiting the room** to prevent exposure, followed by hand hygiene
- After patient transfer or discharge, the room door must be kept closed and the Airborne Precautions sign must remain on the door until sufficient time has elapsed to allow removal of airborne microorganisms (2 hours or as per air changes)

HCW Exposure Management for Measles

- Exposure to measles is considered significant if it involves sharing the same air space, either simultaneously or for up to two hours afterwards, depending on number of air changes, as a clinical case of measles
- Presumptively immune HCWs may continue to work without disruption (2 doses of MMR or laboratory evidence of immunity)
- HCWs who have received one dose of MMR should receive the second dose of MMR* and measles serology (IgG) should be ordered. HCW to be off work awaiting IgG result from Day 5 post-exposure. If IgG positive, HCW will be considered presumptively immune and may continue at work
- If IgG negative consider susceptible and exposed, and work restriction will apply from day 5 from the first exposure until day 21 from the last exposure

*Note women should be advised to delay pregnancy for at least 4 weeks following immunization with MMR vaccine

Susceptible Exposed HCWs

- HCWs with negative measles IgG who never received MMR should receive first dose as soon as possible after exposure
- MMR given within 72 hours of exposure may provide protection after exposure (PEP); when given beyond 72 hours provides protection for subsequent exposures
- If clinical measles does not develop after exposure, a second dose of MMR should be given at least 4 weeks after the first
- HCWs with no documentation of immunity should receive 1 dose of MMR, be considered susceptible and excluded from work; **serology should be performed and if IgG positive may return to work;** if negative, work restrictions apply
- Note work restrictions apply from 5 days after the first exposure until 21 days after the last exposure regardless of whether they received MMR or immune globulin after the exposure

Susceptible Exposed Immunocompromised or Pregnant HCW[25]

- Susceptible exposed HCWs in whom vaccine is contraindicated (e.g., immunocompromised, pregnancy) must be offered human immune globulin within 6 days of exposure to prevent or modify measles
- It is important to consider that Ig only provides short-term protection
- For HCWs who can later receive MMR (e.g., pregnant HCWs), MMR should be postponed 5 to 6 months after Ig is administered
- **Note work restriction extends to 5 days after the first exposure until 28 days after the last exposure**

25. Ontario Hospital Association; Ontario Medical Association. Measles surveillance protocol for Ontario hospitals. Toronto, ON: Ontario Hospital Association; 2019

Acute Disease

HCWs who develop acute disease should be excluded until 4 complete days have passed after onset of rash and they feel well enough to return

Key Points to Remember

- Conduct an ORA to ensure measles readiness for your facility including settings at risk of exposure (e.g., ER, Urgent Care, primary care, paediatric or public health clinics, SCCs), patients at risk (pregnant, under age 5, immunocompromised) and measures to mitigate exposure and transmission
  - Apply the hierarchy of controls including administrative controls (policies, procedures, immunization programs, education and training and correct selection and use of PPE
- Ensure all HCWS are immune to measles through two doses of measles-containing vaccine (MMR) or laboratory evidence regardless of year of birth
- HCWS are to wear a fit-tested, seal-checked N95 respirator and additional PPE based on PCRA when in contact with suspect (period of communicability) or confirmed measles cases, regardless of presumptive immune status

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Questions and Answers

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