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How	Each province or territory will advise which vaccines will be made available for the publicly-funded program in that jurisdiction. Children who have been previously immunized with seasonal influenza vaccine and adults are to receive one dose of influenza vaccine each year. Children 6 months to less than 9 years of age receiving seasonal influenza vaccine for the first time should be given two doses, with a minimum interval of four weeks between doses. The route of administration and dosage varies by product. For intramuscular (IM) TIV, the dose is 0.5 ml for all age groups.
Why	It is estimated that between 10-20% of the population becomes infected with influenza each year. Each year there is a new vaccine to protect against the influenza virus strains that are expected in the coming influenza season. Vaccination is the most effective way to prevent influenza and its complications.

The National Advisory Committee on Immunization (NACI) produces an annual *Statement* regarding seasonal influenza vaccination. Health care providers should consult the current annual *Statement* available at the NACI website for information and recommendations specific to the upcoming influenza season. (http://www.phac-aspc.gc.ca/naci-ccni/index-eng.php)

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Influenza is a respiratory infection caused by influenza A and B viruses. Influenza A viruses are classified into subtypes on the basis of two surface proteins: hemagglutinin (HA) and neuraminidase (NA). Influenza B have evolved into two lineages, B/Yamagata/16/88-like and B/Victoria/2/87-like viruses. Over time, antigenic variation (antigenic drift) of strains occurs within an influenza A subtype or B lineage..

Transmission

Influenza is primarily transmitted by droplets spread through coughing or sneezing and may also be transmitted through direct or indirect contact with contaminated respiratory secretions. The incubation period of seasonal influenza is usually two days but can range from one to four days. Adults may be able to spread influenza to others from one day before symptom onset to approximately five days after symptoms start. Children and people with weakened immune systems may be infectious for longer.

Risk factors

The people at greatest risk of influenza-related complications are adults and children with underlying health conditions, including morbid obesity; residents of nursing homes and other chronic care facilities; people 65 years of age and older; children 6 to 59 months of age; pregnant women; and Aboriginal peoples.

Seasonal/temporal pattern

In Canada, influenza generally occurs each year in the late fall and winter months.

Spectrum of clinical illness

Symptoms typically include the sudden onset of high fever, cough and muscle aches. Other common symptoms include headache, chills, loss of appetite fatigue and sore throat. Nausea, vomiting and diarrhea may also occur, especially in children. Most people will recover within a week or ten days, but some - including those 65 years of age and older and adults and children with chronic conditions - are at greater risk of more severe complications, such as pneumonia.

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DISEASE DISTRIBUTION

Incidence/prevalence

Global

Worldwide, annual epidemics result in an approximately one billion cases of influenza, about three to five million cases of severe illness, and about 250,000 to 500,000 deaths. For current international influenza activity information refer to WHO's FluNet website. (http://www.who.int/influenza/gisrs_laboratory/flunet/en/)

National

Influenza activity in Canada usually is low in the spring and summer, begins to rise over the fall and peaks in the winter months (depending on the year, the peak may occur as early as late fall or as late as early spring). The FluWatch program collects data and information from various sources to provide a national picture of influenza activity. For current influenza activity information refer to PHAC's FluWatch website. (http://www.phac-aspc.gc.ca/fluwatch/index-eng.php)

PREPARATIONS AUTHORIZED FOR USE IN CANADA

Influenza vaccines authorized for use in Canada must meet predetermined immunogenicity and safety criteria or standards set by Health Canada. Influenza vaccine may be administered to anyone ≥6 months of age without contraindications. There are currently eight seasonal trivalent influenza vaccines authorized for use in Canada.

- Agriflu® (Novartis) (TIV)
- Fluad® (Novartis) (TIV)
- FluMist® (AstraZeneca) live attenuated vaccine (LAIV)
- Fluviral® (GlaxoSmithKline) (TIV)
- Fluzone® (Sanofi Pasteur) (TIV)
- Influvac® (Abbott) (TIV)
- Intanza® (Sanofi Pasteur) 9 µg and 15 µg formulations (TIV-ID)
- Vaxigrip® (Sanofi Pasteur) (TIV)

For information about the characteristics of influenza vaccines authorized in Canada refer to the most current Statement on Seasonal Influenza Vaccine. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-4/) For complete prescribing information, consult the product leaflet or information contained within the Health Canada's authorized product monographs available through Health Canada's Drug Product Database. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Each province or territory will advise which vaccines will be made available for the publicly-funded program in their jurisdiction.

TRIVALENT INACTIVATED INFLUENZA VACCINE (TIV)

The seven TIV products currently authorized for use in Canada are a mix of split virus and subunit vaccines, which are standardized to contain the same HA content. In split virus vaccines, the virus has been disrupted by a detergent. In subunit vaccines, HA and NA have been further purified by removal of other viral components. The amount of NA in the vaccines is not standardized. Refer to Basic Immunology and Vaccinology in Part 1for more information about inactivated vaccines.

One of the TIV products, Fluad®, contains the adjuvant MF59, which is an oil-in-water emulsion composed of squalene as the oil phase, stabilized with the surfactants polysorbate 80 and sorbitan triolate in citrate buffer. The other six TIV products do not contain an adjuvant.

One of the TIV products (Intanza®) is administered intra-dermally; the other six TIV products are administered intramuscularly.

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LIVE ATTENUATED INFLUENZA VACCINE (LAIV)

FluMist® is a live attenuated influenza vaccine for administration by intranasal spray and authorized for use for persons 2-59 years of age. Each 0.2 mL dose of FluMist®, (given as 0.1 mL in each nostril) contains $10^{6.5-7.5}$ fluorescent focus units (FFU) of live attenuated virus reassortants of each of three strains propagated in pathogen-free eggs. The influenza strains in FluMist® are cold-adapted and temperature sensitive, so they replicate in the nasal mucosa rather than the lower respiratory tract, and they are attenuated so they do not produce classic influenza-like illness.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

Multiple studies show that influenza vaccine is efficacious with higher efficacy demonstrated against laboratory-confirmed influenza than clinically defined outcomes. In healthy children (equal to or younger than 18 or 16 years old) a systematic review and meta-analyses showed that efficacy of influenza vaccine against laboratory confirmed influenza ranged from 59% to 82%, efficacy against serologically-confirmed influenza ranged from 54% to 63% and efficacy against clinical illness ranged between 33% to 36%. In a systematic review, for healthy adults, inactivated influenza vaccine efficacy against laboratory-confirmed influenza was 80% (95% CI, 56 to 91) and vaccine effectiveness against influenza-like illness was 30% (95% CI, 17 to 41) when the vaccine strain matched the circulating strains and circulation was high. Another meta-analysis identified vaccine efficacy of 50% in healthy adults (95% CI, 27 to 65) during select seasons of vaccine mismatch, although mismatch is a relative term and the amount of cross-protection is expected to vary. In the elderly, vaccine effectiveness is about half of that of healthy adults and varies depending on the outcome and the study population.

In observational studies, immunization has been shown to reduce the number of physician visits, hospitalizations and deaths in high-risk persons 18 to 64 years of age, hospitalizations for cardiac disease and stroke in the elderly, and hospitalization and deaths in persons with diabetes mellitus 18 years of age and older.

For a summary of efficacy studies refer to the most recent NACI seasonal influenza statement.

IMMUNOGENICITY

The antigenic components of the vaccine may change each year. Because influenza viruses change over time, immunity conferred in one season will not reliably prevent infection by an antigenically drifted strain. Even if the vaccine strains have not changed, immunity generally wanes within a year of receiving the vaccine and re-immunization reinforces optimal protection for the coming influenza season.

The antibody response after vaccination depends on several factors, including the age of the recipient, prior and subsequent exposure to antigens and the presence of immune compromising conditions. Humoral antibody levels, which correlate with vaccine protection, are generally achieved by two weeks after immunization; however, there may be some protection afforded before that time.

RECOMMENDATIONS FOR USE

Influenza vaccine may be administered to anyone 6 months of age and older without contraindications. Decisions regarding the precise timing of vaccination in a given setting or geographic area should be made according to local epidemiologic factors (influenza activity, timing and intensity), opportune moments for vaccination, as well as programmatic issues.

With the variety of influenza vaccines that are now available, it is important for practitioners to note the specific differences in age indications, route of administration, dosage and schedule for the products that they will be using (Table 3). Characteristics of influenza vaccines authorized in Canada are available in Contents of Immunizing Agents Available for Use in Canada in Part and the most recent NACI seasonal influenza statement.

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RECOMMENDED RECIPIENTS OF INFLUENZA VACCINE

To reduce the morbidity and mortality associated with influenza, immunization programs should **focus** on those at high risk of influenza-related complications, those capable of transmitting influenza to individuals at high risk of complications and those who provide essential community services (refer to Table 1). Healthy persons aged 5 to 64 years who do not have contraindications to influenza vaccine are also encouraged to receive influenza vaccine even if they are not in one of the recommended recipient groups.

Table 1: Recommended recipients of influenza vaccine for the 2013-2014 season[1]

People at high risk of influenza-related complications or hospitalization

- Adults (including pregnant women) and children with the following chronic health conditions:
  - cardiac or pulmonary disorders (including bronchopulmonary dysplasia, cystic fibrosis and asthma);
  - diabetes mellitus and other metabolic diseases;
  - cancer, immune compromising conditions (due to underlying disease and/or therapy);
  - renal disease;
  - anemia or hemoglobinopathy;
  - conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration;
  - morbid obesity (BMI≥40); and
  - children and adolescents with conditions treated for long periods with acetylsalicylic acid.
- People of any age who are residents of nursing homes and other chronic care facilities.
- People ≥65 years of age.
- All children 6 to 59 months of age.
- Healthy pregnant women (the risk of influenza-related hospitalization increases with length of gestation, i.e. it is higher in the third than in the second trimester)
- Aboriginal peoples.

People capable of transmitting influenza to those at high risk

- Health care and other care providers in facilities and community settings who, through their activities, are capable of transmitting influenza to those at high risk of influenza complications.
- Household contacts (adults and children) of individuals at high risk of influenza-related complications (whether or not the individual at high risk has been immunized):
  - household contacts of individuals at high risk, as listed in the section above;
  - household contacts of infants <6 months of age as these infants are at high risk of complications from influenza but cannot receive influenza vaccine; and
  - members of a household expecting a newborn during the influenza season.
- Those providing regular child care to children ≤59 months of age, whether in or out of the home.
- Those who provide services within closed or relatively closed settings to persons at high risk (e.g. crew on a ship).

Others

- People who provide essential community services.
- People in direct contact during culling operations with poultry infected with avian influenza.

[1] Healthy persons aged 5 to 64 years who do not have contraindications to influenza vaccine are also encouraged to receive influenza vaccine even if they are not in one of the recommended recipient groups.

PREGNANCY AND BREASTFEEDING

All pregnant women, at any stage of pregnancy, should be included among high priority recipients of influenza vaccine due to the risk of influenza-associated morbidity in pregnant women, evidence of adverse neonatal outcomes associated with maternal respiratory hospitalization or influenza during pregnancy, evidence that vaccination of pregnant women protects their newborns from influenza and

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influenza-related hospitalization, and evidence that infants born during influenza season to vaccinated women are less likely to be premature, small for gestational age, and low birth weight.

Both TIV and TIV-ID (9 µg) are available for use in pregnant women and there is no preference for the use of either product. Due to a lack of safety data at this time, LAIV, which is a live attenuated vaccine, should not be administered to pregnant women, but it can be administered to breastfeeding women. Refer to Immunization in Pregnancy and Breastfeeding in Part 3 for additional information.

IMMUNOCOMPROMISED PERSONS

Influenza vaccination can induce protective antibody levels in a substantial proportion of adults and children with immune compromising conditions, including transplant recipients, those with proliferative diseases of the hematopoietic and lymphatic systems, and HIV-infected persons. Vaccine efficacy may be lower in persons with immune compromising conditions than in healthy adults. LAIV is not recommended for people with immune compromising conditions. If TIV-ID is being used for adults with immune compromising conditions, the 15 µg formulation should be considered to improve response.

Close contacts

LAIV recipients should avoid close association with persons with severe immune compromising conditions (e.g., bone marrow transplant recipients requiring isolation) for at least two weeks following vaccination, because of the theoretical risk for transmission. Refer to Immunization of Immunocompromised Persons in Part 3 for additional information.

TRAVELLERS

Influenza occurs year-round in the tropics. In temperate northern and southern countries, influenza activity peaks generally during the winter season (November to March in the Northern Hemisphere and April to October in the Southern Hemisphere). Influenza vaccination is recommended for travellers with a chronic health condition or other factors that would make them part of the recommended recipients of influenza vaccine due to increased risk of complications following influenza infection. In addition, influenza immunization is encouraged for all Canadians over 6 months of age which would also apply to travellers.

Vaccines prepared specifically for use in the Southern Hemisphere are not available in Canada, and the extent to which recommended vaccine components for the Southern Hemisphere may overlap with those in available Canadian formulations will vary. A decision in favour or against re-vaccination (i.e., boosting) of travellers to the Southern Hemisphere between April and October if they had already been vaccinated in the preceding fall/winter with the Northern Hemisphere vaccine depends on individual risk assessment, the similarity or differences between the Northern and Southern hemisphere vaccines, and the availability of a reliable and safe vaccine at the traveller's destination. For further information on advising travellers about influenza prevention, consult the Committee to Advise on Tropical Medicine and Travel (CATMAT) website. (http://www.phac-aspc.gc.ca/tmp-pmv/catmat-ccmtmv/) Refer to Immunization of Travellers in Part 3 for additional general information.

CHOICE OF SEASONAL INFLUENZA VACCINE

With the recent authorization of a number of new vaccines, some of which are designed to enhance immunogenicity in specific age groups, the choice of product is no longer straightforward.
The decision to include specific influenza vaccines as part of publicly-funded provincial/territorial programs depends on multiple factors such as cost-benefit evaluation and other programmatic and operational factors, such as shelf-life and implementation strategies. Not all products will be made available in all jurisdictions and availability of some products may be limited, vaccine providers should consult their province or territory for specifics on the products provided in their jurisdiction. Table 2 summarizes current recommendations for the choice(s) of influenza vaccine in specific age and risk groups.

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Table 2: Choice of influenza vaccine for selected age and risk groups (for persons without a contraindication to the vaccine)

Recipient by age group	Vaccine types available for use	Preferred vaccine for healthy persons	Preferred vaccine for persons with chronic health conditions	Comments
Children 6–23 months of age	TIV	-	-	Only TIV is available for this age group
Children 2–17 years of age	TIV LAIV	LAIV[1]	No preference	Children with immune compromising conditions: • LAIV not recommended
Adults 18–59 years of age	TIV TIV-ID (9 µg) LAIV	No preference	TIV TIV-ID (15 µg)[2]	Adults with immune compromising conditions: • LAIV not recommended
Adults 60–64 years of age	TIV TIV-ID (15 µg)	No preference	No preference	
Adults 65+ years of age	TIV TIV-ID (15 µg) MF59-adjuvanted TIV	No preference	No preference	
Pregnant women	TIV TIV-ID (9 µg)	No preference	No preference	LAIV not recommended

TIV = trivalent inactivated influenza vaccine (for IM administration)
TIV-ID = trivalent inactivated influenza vaccine for intradermal injection
LAIV = live attenuated influenza vaccine

[1] Unless contraindicated, there is evidence for the preferential use of LAIV in young children (younger than 6 years of age) based on superior efficacy of LAIV compared to TIV, with weaker evidence of superior efficacy in older children. It is anticipated that the superior efficacy for LAIV over TIV extends beyond age 6 years, but the evidence does not indicate at which specific age the efficacies of LAIV and TIV become equivalent.

[2] With TIV-ID, consider the 15 µg formulation for adults with immune compromising conditions.

VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

The recommended dosage schedule for the authorized products is presented in Table 3. Children 6 to 35 months of age should be given a full dose (0.5 mL) of TIV as is recommended for older children and adults. The first time children 6 months to less than 9 years of age receive seasonal influenza vaccine, whether TIV or LAIV, a two-dose schedule is required with a minimum interval of four weeks between doses. Pending further evidence, eligible children less than 9 years of age who have previously received one or more doses of seasonal influenza vaccine should receive one dose per influenza vaccination season thereafter.

The recommended injection site for TIV-ID, which is given intradermally using the supplied micro-injection device, is the deltoid region. LAIV is intended for intranasal administration only and should not be administered by the IM or ID route. It is supplied in a pre-filled single use sprayer containing 0.2 mL of vaccine. Approximately 0.1 mL (one-half) is sprayed into the first nostril with the recipient upright, then the dose divider clip is removed and the remainder of the vaccine (0.1 mL) is sprayed into the other nostril. Refer to Vaccine Administration Practices in Part 1 and the manufacturer's instructions available in the product leaflet and product monograph for additional information.

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Table 3: Influenza vaccine: Recommended dosage and route, by age, for the 2013-2014 season

Age group	TIV without adjuvant[1] IM	MF59 -adjuvanted TIV (Fluad®) IM	TIV for intradermal use (Intanza®) ID	LAIV (FluMist®)[2] IN	Number of doses required
6–23 months	0.5 mL[3]	-	-	-	1 or 2[4]
2–8 years	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1 or 2[4]
9–17 years	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1
18–59 years	0.5 mL	-	0.1 mL (9 µg/strain)[5]	0.2 mL (0.1 mL per nostril)	1
60–64 years	0.5 mL	-	0.1 mL (15 µg/strain)	-	1
≥65 years	0.5 mL	0.5 mL	0.1 mL (15 µg/strain)	-	1

TIV = Trivalent inactivated vaccine
LAIV = Live attenuated influenza vaccine
IM= intramuscular
ID= Intradermal
IN = intranasal

[1] Influvac® ≥18 years; Fluviral® ≥6 months; Agriflu® ≥6 months; Vaxigrip® ≥6 months; and Fluzone® ≥6 months
[2] Unless contraindicated, there is evidence for the preferential use of LAIV in young children (younger than 6 years of age) based on superior efficacy of LAIV compared to TIV, with weaker evidence of superior efficacy in older children. It is anticipated that the superior efficacy for LAIV over TIV extends beyond age 6 years, but the evidence does not indicate at which specific age the efficacies of LAIV and TIV become equivalent.
[3] This information differs from the product monograph. Recommendations for use and other information in this *Guide* may differ from that set out in the product monographs/leaflets of the Canadian manufacturers.
[4] Children 6 months to less than 9 years of age who have never received the seasonal influenza vaccine require two doses of influenza vaccine, with a minimum interval of four weeks between doses. Eligible children less than 9 years of age who have properly received one or more doses of seasonal influenza vaccine in the past should receive one dose per influenza vaccination season thereafter.
[5] For adults with immune compromising conditions, the 15µg formulation should be considered to improve response.

BOOSTER DOSES AND RE-IMMUNIZATION

Booster doses are not recommended within the same influenza season.

SEROLOGICAL TESTING

Serologic testing is not recommended before or after receiving seasonal influenza vaccine.

STORAGE REQUIREMENTS

Influenza vaccine should be stored at +2°C to +8°C and should not be frozen. Refer to the individual product monographs for further details. Refer to Storage and Handling of Immunizing Agents in Part 1 for additional information.

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SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

All influenza vaccines, including LAIV, may be given concomitantly with or at any time before or after live attenuated vaccines or inactivated vaccines. When administering two or more parenteral vaccines, different administration sets (needle and syringe) should be used for each injection. Refer to Timing of Vaccine Administration in Part 1 for additional information.

The target groups for influenza and pneumococcal polysaccharide vaccines overlap considerably. Health care providers should take the opportunity to vaccinate eligible persons against pneumococcal disease when influenza vaccine is given.

VACCINE SAFETY AND ADVERSE EVENTS

Influenza vaccine is safe and well-tolerated and may be given to persons starting from six months of age (noting product-specific age indications and contraindications). Refer to Vaccine Safety Part 2 for additional information.

COMMON AND LOCAL ADVERSE EVENTS

TIV

With IM products, soreness at the injection site lasting up to two days is common in adults but rarely interferes with normal activities. Healthy adults receiving TIV show no increase in the frequency of fever or other systemic symptoms compared with those receiving placebo. TIV is safe and well tolerated in healthy children. Mild injection site reactions, primarily soreness at the vaccination site, occur in 7% or less of healthy children who are less than 3 years of age. Post-vaccination fever may be observed in 12% or less of immunized children 1 to 5 years of age.

MF59-adjuvanted TIV (Fluad®) produces injection site reactions (pain, erythema and induration) significantly more frequently than non-adjuvanted vaccines, but they are classified as mild and transient. Systemic reactions (myalgia, headache, fatigue and malaise) are comparable or more frequent with Fluad® compared to non-adjuvanted vaccines and are rated as mild to moderate and transient.

TIV-ID produces more frequent and more extensive erythema, swelling, induration and pruritus than vaccine given by the IM route. These reactions are generally mild and resolve spontaneously within a few days. Systemic reactions following TIV-ID are comparable to IM vaccine, except for myalgia which is less common with TIV-ID.

LAIV

The most common adverse events experienced by LAIV recipients are nasal congestion and runny nose.

LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. Allergic responses to influenza vaccine are a rare consequence of hypersensitivity to some vaccine components. Refer to Contraindications and Precautions for additional information.

OTHER REPORTED ADVERSE EVENTS AND CONDITIONS

Guillain-Barré syndrome (GBS)

Recent studies suggest that the absolute risk of GBS in the period following seasonal and A(H1N1)pdm09 influenza vaccination is about one excess case per 1 million vaccines. Refer to Contraindications and Precautions for additional information.

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Oculo-respiratory syndrome (ORS)

Oculorespiratory syndrome (ORS), defined as the onset of bilateral red eyes and/or respiratory symptoms (cough, wheeze, chest tightness, difficulty breathing, difficulty swallowing, hoarseness or sore throat) and/or facial swelling occurring within 24 hours of influenza immunization, was found during the 2000-2001 influenza season; few cases have been reported since then. It is not considered to be an allergic response.

Persons who have a recurrence of ORS upon revaccination do not necessarily experience further episodes with future vaccinations. Data on clinically significant adverse events do not support the preference of one vaccine product over another when revaccinating those who have previously experienced ORS. Refer to Contraindications and Precautions for additional information.

GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Vaccine providers are asked to report through local public health officials any serious or unexpected adverse event felt to be temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI. The following AEFIs are of particular interest:

- Oculorespiratory Syndrome (ORS)
- Guillain-Barré Syndrome (GBS) within 6 weeks following immunization

Refer to Vaccine Safety in Part 2 and the national Adverse Events Following Immunization Report Form (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and the User Guide to the Completion and Submission of the AEFI Reports (http://www.phac-aspc.gc.ca/im/aefi-essi_guide/index-eng.php) for additional information about AEFI reporting.

CONTRAINDICATIONS

Influenza vaccine should not be given to:

- people who have had an anaphylactic reaction to a previous dose; or
- people who have had an anaphylactic reaction to any of the vaccine components, with the exception of egg.

Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for a list of all vaccines available for use in Canada and their contents.

Additional LAIV - specific contraindications

LAIV should not be administered to:

- Children less than 24 months of age due to increased risk of wheezing.
- Individuals with severe asthma (as defined as currently on oral or high dose inhaled glucocorticosteriods or active wheezing) or those with medically attended wheezing in the 7 days prior to vaccination.
- Children and adolescents (2 to 17 years of age) currently receiving aspirin or aspirin-containing therapy because of the association of Reye's syndrome with aspirin and wild-type influenza infection. It is recommended that aspirin-containing products in children less than 18 years of age be delayed for four weeks after receipt of LAIV.
- Pregnant women, because it is a live attenuated vaccine and there is a lack of safety data at this time. However, it is not contraindicated in breastfeeding mothers.
- Persons with immune compromising conditions, due to underlying disease and/or therapy, as the vaccine contains live attenuated virus.

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PRECAUTIONS

Allergic reactions to previous vaccine doses

Expert review of the risks and benefits of vaccination should be sought for those who have previously experienced severe lower respiratory symptoms (wheeze, chest tightness, difficulty breathing) within 24 hours of influenza vaccination, an apparent significant allergic reaction to the vaccine or any other symptoms (e.g., throat constriction, difficulty swallowing) that raise concern regarding the safety of re-immunization. This advice may be obtained from local medical officers of health or other experts in infectious disease, allergy/immunology and/or public health.

In view of the considerable morbidity and mortality associated with influenza, a diagnosis of influenza vaccine allergy should not be made without confirmation (which may involve skin testing) from an allergy/immunology expert. Individuals who have an allergy to substances that are not components of the influenza vaccine are not at increased risk of allergy to influenza vaccine.

Oculo-respiratory syndrome (ORS)

Individuals who have experienced ORS without lower respiratory tract symptoms - may be safely re-immunized with influenza vaccine. Persons who experienced ORS with lower respiratory tract symptoms should have an expert review. Health care providers who are unsure whether an individual previously experienced ORS versus an IgE-mediated hypersensitivity immune response should seek advice.

Guillain-Barré syndrome (GBS)

Although the evidence considering influenza vaccination and GBS was inadequate to accept or reject a causal relation between GBS in adults and seasonal influenza vaccination, avoiding subsequent influenza vaccination of persons known to have had GBS within six weeks of a previous influenza vaccination appears prudent at this time. However, the potential risk of GBS recurrence associated with influenza vaccination must be balanced against the risk of GBS associated with influenza infection itself.

Severe acute illness with or without fever

Administration of seasonal influenza vaccine should usually be postponed in persons with serious acute illness until their symptoms have abated. Immunization should not be delayed because of minor acute illness, with or without fever. If significant nasal congestion is present that might impede delivery of LAIV to the nasopharyngeal mucosa, TIV can be administered or LAIV could be deferred until resolution of the illness.

Additional LAIV - specific precautions

LAIV recipients should avoid close association with persons with severe immune compromising conditions (e.g., bone marrow transplant recipients requiring isolation) for at least two weeks following vaccination, because of the theoretical risk for transmitting a vaccine virus and causing infection.

ADMINISTRATION OF INFLUENZA VACCINE TO EGG ALLERGIC PERSONS

All influenza vaccine products are manufactured by a process involving chicken eggs, which may result in the vaccine containing trace amounts of residual egg protein.

Egg-allergic individuals may be vaccinated against influenza using TIV, without prior influenza vaccine skin test and with the full dose, irrespective of a past severe reaction to egg, with the following conditions. Those with mild reactions such as hives, or those who tolerate eggs in baked goods may be vaccinated in regular vaccination clinics. Those who have suffered from anaphylaxis with respiratory or cardiovascular symptoms should be vaccinated in a medical clinic, allergy office or hospital where appropriate expertise and equipment to manage respiratory or cardiovascular compromise is present. These individuals should always be kept under observation for 30 minutes.

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Referral to a specialist with expertise in allergies may be necessary in occasional circumstances where there is strong concern about proceeding with the recommendation above and the individual is at risk of complications from influenza. If the individual is not in a high-risk group, the need for vaccination may be reassessed.

Data are not currently available to support this recommendation for LAIV.

Refer to Anaphylactic Hypersensitivity to Egg and Egg-Related Antigens in Part 2 for additional information.

DRUG INTERACTIONS

Although influenza vaccine can inhibit the clearance of warfarin and theophylline, clinical studies have not shown any adverse effects attributable to these drugs in people receiving influenza vaccine. It is recommended that LAIV not be administered until 48 hours after antiviral agents active against influenza (oseltamivir and zanamivir) are stopped, and that antiviral agents not be administered until two weeks after receipt of LAIV unless medically indicated. If antiviral agents are administered within this time frame (from 48 hours before to two weeks after LAIV is given), revaccination should take place at least 48 hours after the antivirals are stopped.

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PART 4

JAPANESE ENCEPHALITIS VACCINE

KEY INFORMATION (refer to text for details)

What	• Japanese encephalitis (JE) virus is transmitted to humans primarily through the bite of an infected mosquito. • JE occurs in many areas of Asia, especially in the south east and in parts of the western Pacific, and is the leading cause of viral encephalitis in Asia. • Transmission of JE virus occurs primarily in rural agricultural areas. • The risk for acquiring JE is low for most travellers, particularly for short-term visitors to major urban areas. • Most JE infections are asymptomatic. Only a small percentage of people infected with JE virus develop clinical disease. • When encephalitis occurs, it is usually severe, with 20% to 30% mortality rates and residual neuropsychiatric problems in 30% to 50% of survivors. • The most commonly reported adverse events following JE vaccination are injection site tenderness, redness and hardening; headache; myalgia; and fatigue.
Who	• JE vaccine is recommended for adult travellers with a high exposure risk going to JE endemic/epidemic areas during the transmission season and for laboratory personnel who work with JE virus. • JE vaccine is not authorized for use in children less than 18 years of age but may be considered in high risk circumstances.
How	• Give JE vaccine as two separate 0.5 mL doses on days 0 and 28.
Why	• When encephalitis occurs, it is usually severe, with 20% to 30% mortality rates and residual neuropsychiatric problems in 30% to 50% of survivors. • Short-term (less than 1 month) travellers whose visits are restricted to major urban areas are at minimal risk for JE.

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Since the publication of *2006 Canadian Immunization Guide:*

- An inactivated Vero cell culture-derived Japanese encephalitis (JE) vaccine with a revised dosing schedule has become available for persons 18 years of age and older.
- Inactivated mouse brain-derived JE vaccine (JE-VAX® [Sanofi Pasteur Ltd.]) is no longer available in Canada.
- In Canada, JE vaccine is not authorized for use in persons less than 18 years of age.

For additional information, refer to the Committee to Advise on Tropical Medicine and Travel (CATMAT) *Statement on protection against Japanese encephalitis*. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/08vol34/acs-4/index-eng.php)

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Japanese encephalitis (JE) is caused by a ribonucleic acid (RNA) virus from the family *Flaviviridae*.

Reservoir

The virus in primarily maintained in an enzootic cycle that typically involves the *Culex* mosquito and wild birds. Secondary epizootic cycles can lead to infections of humans, often with domestic pigs as an amplifying host.

Transmission

JE virus is transmitted to humans primarily through the bite of an infected mosquito. Mosquitoes acquire the virus from infected hosts (e.g., pigs and wild birds) and then transmit the virus to non-infected hosts (e.g., humans and horses). The principal vectors are *Culex* species mosquitoes that tend to bite in the evening and night. So called day-biting species predominate in some regions, but they not only bite in the day; they can also bite during the afternoon or evening.

Larvae of *Culex* mosquitoes develop in standing water, such as rice fields. Thus, transmission of JE virus occurs primarily in rural agricultural areas where flooding irrigation is practised; however, cases have been occasionally reported from urban areas.

Humans usually do not develop sufficient viremia to infect mosquitoes, and direct person-to-person spread of JE does not occur except, rarely, through intrauterine transmission. Based on experience with similar viruses, transmission could theoretically occur through blood transfusions or organ transplantation. The incubation period is 5 to 15 days.

Risk factors

A traveller's risk for acquiring JE is determined by multiple factors, including immunization status, use of protective measures against mosquito bites, location of travel, duration of exposure, season, and activities while travelling. The risk for acquiring JE is low for most travellers, particularly for short-term visitors to major urban areas. Greater risk exists for travellers who are:

- visiting rural agricultural areas associated with rice production and flooding irrigation;
- staying for a long time; and
- participating in outdoor activities such as camping, hiking, cycling or fieldwork, especially during the evening or night.

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Seasonal/temporal pattern

In most temperate areas of Asia, JE virus transmission is seasonal and disease usually peaks in summer and fall. In the subtropics and tropics, transmission patterns vary and cases can occur sporadically or year-round.

Spectrum of clinical illness

Most JE infections are asymptomatic. Only a small proportion of people infected with JE will develop clinical symptoms. Less than 1% of people infected with JE virus develop clinical disease. In endemic areas, disease occurs primarily in children.

Acute encephalitis is the most commonly identified clinical syndrome with JE virus infection. When encephalitis occurs, it is usually severe, with 20% to 30% mortality rates and residual neuropsychiatric problems in 30% to 50% of survivors. Milder forms of disease can occur and are reported more commonly among adults. JE acquired during pregnancy carries the risk of intrauterine infection and miscarriage.

DISEASE DISTRIBUTION

Incidence/prevalence

Global

JE occurs in many areas of Asia, especially in the south east and in parts of the western Pacific, and is an important cause of viral encephalitis in Asia. The World Health Organization (WHO) estimates that more than 50,000 JE cases occur annually, with 10,000 deaths and 15,000 cases of long-term neuropsychiatric sequelae. The incidence of JE varies widely from year to year and between regions within countries. In endemic areas, JE usually affects children living in rural areas. However, even in countries with effective childhood JE immunization programs, JE may present a risk to non-immune travellers because transmission is maintained in an enzootic (i.e., wildlife) cycle.

The overall risk for JE among persons from non-endemic countries travelling to Asia is estimated to be less than one case per 1 million travellers. However, the risk for JE among persons who stay for prolonged periods in rural areas with active JE virus transmission may reach levels similar to that of the susceptible resident population (1.2 to 2 cases per 100,000 per week). Short-term (less than 1 month) travellers whose visits are restricted to major urban areas are at minimal risk for JE although rare case reports suggest that even short-term, resort-based travellers can occasionally contract JE. There have been few cases of JE reported among Western travellers.

View a map of the areas at risk for JE transmission is available through the United States Centers for Disease Control and Prevention (CDC) (http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/japanese-encephalitis.htm) or the World Health Oganization(WHO). (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_JE_ITHRiskMap.png)

Japanese encephalitis has been known to occur in many countries, including China, India, Indonesia, Thailand and Vietnam. Risk can vary within areas and at time of year. In addition, JE risk may change over time. It is recommended that travel health practitioners access up-to-date risk information through the United States Centers for Disease Control and Prevention (CDC) Infectious Disease Related to Travel at: or the most current version of the CDC's Health Information for International Travel Yellow Book. (http://wwwnc.cdc.gov/travel/page/yellowbook-2012-home.htm)

National

To date, there has been one possible case of JE reported in a Canadian returning from Asia in 1982.

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PREPARATIONS AVAILABLE FOR USE IN CANADA

JAPANESE ENCEPHALITIS VACCINE

- IXIARO® (Inactivated, Japanese encephalitis vaccine, Vero cell culture-derived, adsorbed). Intercell AG (manufacturer), Novartis Pharmaceuticals Canada Inc.(distributor) (JE)

For complete prescribing information, consult the product leaflet or information contained within Health Canada's authorized product monographs available through the *Drug Product Database*. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Refer to *Table 1* in Contents of Immunizing Agents Available in Canada in Part 1 for a list of all vaccines available for use in Canada and their contents.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

No efficacy or effectiveness data exist for the Vero cell culture-derived JE vaccine, IXIARO®. IXIARO® was authorized for use based on non-inferiority of serologic response compared to the previous mouse brain-derived JE vaccine and to the WHO threshold for protective antibody titre.

IMMUNOGENICITY

A single dose of JE vaccine induces sufficient protective antibodies in 30% of vaccinees at 10 days after vaccination and in 40% of vaccinees at 28 days post-vaccination. A second dose of vaccine given at 28 days after the first dose induces antibodies in about 95% of vaccinees at 28 days after the second dose. Vaccination with two doses of vaccine at the same time may increase the seroconversion rate to 60% at 10 days post-vaccination. The protective antibody concentration declines over time with 80% to 95% of fully immunized vaccinees maintaining an adequate concentration at 6 months after the first dose and 60% to 80% maintaining adequate antibodies at 12 months after the first dose. A booster dose of vaccine, among those who have completed a properly spaced primary series, induces an adequate antibody concentration in those who have lost protective antibodies at 12 months after their first dose.

RECOMMENDATIONS FOR USE

JE vaccine is only one part of the prevention strategy for Japanese encephalitis. All travellers going to JE endemic areas should be advised regarding personal protective measures. These measures may be sufficient to reduce an already small risk of JE to a level at which JE vaccine provides little added benefit. For additional information on alternative preventive tactics and strength of recommendations for vaccination, refer to CATMAT Statement on protection against Japanese encephalitis. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/08vol34/acs-4/index-eng.php)

INFANTS AND CHILDREN

JE vaccine is not authorized for use in persons less than 18 years of age due to little safety and efficacy data in this population. The pediatric traveller, especially the longer-term traveller, to areas endemic for JE may be at risk for JE infection and serious complications. If travel cannot be avoided or deferred, travellers less than 18 years of age should be advised to diligently use protective measures to prevent mosquito bites. When a child will be spending a prolonged period of time in an area at risk of acquisition, parents should be informed about the risk of disease occurring; the possibility of the child receiving a WHO approved JE vaccine at the destination should be explored; and the risk and benefits of receiving the vaccine "off-label" in Canada prior to departure presented. Data from a small study of children vaccinated with 2 doses of IXIARO® demonstrated protective antibody response similar to adults and without unexpected adverse events. Preliminary data suggest the use of a half adult dose in children less than 3 years of age.

ADULTS (18 years of age and older)

JE vaccine is recommended for travellers to JE endemic/epidemic areas during the transmission season who will:

- spend more than a cumulative total of 30 days in rural areas during the season of risk (or in urban areas known to be endemic or epidemic for JE); including longer-term travellers or expatriates who, while based in urban areas, anticipate making intermittent short trips to rural areas of risk.
- spend less than a cumulative total of 30 days in rural areas during the season of risk (or in urban areas known to be endemic or epidemic for JE) if substantial activity outdoors (or indoors if the indoor area does not exclude mosquitoes) is anticipated, especially during the evening/night.

JE vaccine is generally not recommended for travellers to JE endemic/epidemic areas during the transmission season whose:

- entire itinerary will be in urban areas (unless the urban areas are known to be endemic or epidemic for JE).
- visits to rural areas (or urban areas known to be endemic or epidemic for JE) will be during the daytime only.

JE vaccine is recommended for laboratory personnel who work with JE virus.

Refer to *Schedule* for additional information.

PREGNANCY AND BREASTFEEDING

There are no data related to safety or efficacy of JE vaccine in pregnant or lactating women. Pregnant or lactating women who must travel to areas where the risk of JE infection is high should be immunized only if the risk of disease outweighs the unknown risk of vaccination to the woman and/or her fetus/breastfeeding infant. Refer to *Immunization in Pregnancy and Breastfeeding* in Part 3 for additional general information.

IMMUNOCOMPROMISED PERSONS

If travel must be undertaken, immunocompromised persons may be immunized with JE vaccine; however, the antibody response may be suboptimal and the person should be advised to be diligent about mosquito protection measures. When considering immunization of an immunocompromised person, consultation with the individual's attending physician may be of assistance. For complex cases, referral to a physician with expertise in immunization and/or immunodeficiency is advised.

Refer to Immunization of Immunocompromised Persons in Part 3 for additional general information.

WORKERS

Laboratory personnel who work with JE virus should receive JE vaccine. Refer to Immunization of Workers in Part 3 for additional general information.

VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

Dose

Each dose is 0.5 mL.

Route of administration

JE vaccine should be administered intramuscularly. Refer to *Vaccine Administration Practices* in Part 1 for additional information.

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Schedule

A series of two doses given on days 0 and 28 should be administered. The immunization series should be completed 10 to 14 days before potential exposure to JE to develop an adequate antibody response. An accelerated schedule is not available. However, if there is insufficient time to administer the recommended two-dose schedule before entering a JE risk situation, a single dose of JE vaccine may be considered and the vaccinee advised that protection against JE may not be reliable. Alternatively, simultaneous administration of two doses of JE vaccine (given with separate injections at separate injection sites) may be considered; however, the risks and benefits of this approach must be critically evaluated.

BOOSTER DOSES AND RE-IMMUNIZATION

A booster dose (third dose) should be given one year after the second dose in the primary series, when there is a potential for re-exposure to JE virus. Persons at continuous risk for acquiring JE (laboratory personnel or persons residing in endemic areas) should receive a booster dose 12 months after primary immunization. Data on the need for further booster doses are not available. If a person received the previous mouse brain-derived JE vaccine more than 3 years ago and requires re-immunization, a two dose primary series of the currently available Vero cell culture-derived JE vaccine (IXIARO®) should be administered.

SEROLOGICAL TESTING

Serologic testing is not recommended before or after receiving JE vaccine.

STORAGE REQUIREMENTS

Store JE vaccine in a refrigerator at +2°C to +8°C. Do not freeze. Protect from light. Refer to *Storage and Handling of Immunizing Agents* in Part 1 for additional general information.

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

Data are limited regarding the safety and immunogenicity of JE vaccine when given concomitantly with other vaccines. In general, inactivated vaccines, such as JE vaccine, can be given concurrently with any other vaccine using different injection sites and separate needles and syringes. JE vaccine has been given concomitantly with hepatitis A vaccine without significant interference with safety and immunogenicity. There are no data available regarding possible interference between JE vaccine and yellow fever vaccine. Refer to Timing of Vaccine Administration in Part 1 for additional general information.

VACCINE SAFETY AND ADVERSE EVENTS

Refer to *Vaccine Safety* Part 2 for additional general information.

COMMON AND LOCAL ADVERSE EVENTS

Tenderness or pain (about 34.0%), redness (9.1%) and hardening (8.0%) are the most common vaccination site reactions following JE vaccination. Common systemic side effects include headache (19.2%), myalgia (13.4%), fatigue (9.5%) and influenza-like illness (8.8%). Other reactions, such as vaccination site swelling or itching, rash, fever, and nausea are reported in 1% to 5% of vaccinees.

LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. Anaphylaxis following vaccination with JE vaccine may occur but is very rare. No serious hypersensitivity reactions or neurologic adverse events have been identified among JE vaccine recipients enrolled in clinical trials.

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GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Vaccine providers are asked to report, through local public health officials, any serious or unexpected adverse event felt to be temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization or a change in the frequency of a known AEFI. Refer to *Reporting Adverse Events Following Immunization (AEFI) in Canada* (http://www.phac-aspc.gc.ca/im/aefi-essi_guide/index-eng.php) in Vaccine Safety in Part 2 for additional information about AEFI reporting.

CONTRAINDICATIONS AND PRECAUTIONS

JE vaccine is contraindicated in persons with history of anaphylaxis after previous administration of the vaccine and in persons with proven immediate or anaphylactic hypersensitivity to any component of the vaccine or its container. The vaccine does not contain any preservatives. Refer to *Table 1* in Contents of Immunizing Agents Available in Canada in Part 1 for lists of all vaccines available for use in Canada and their contents.

Administration of JE vaccine should be postponed in persons with moderate or severe acute illness. Persons with minor acute illness (with or without fever) may be vaccinated.

Refer to General Contraindications and Precautions in Part 2 for additional general information.

OTHER CONSIDERATIONS

INTERCHANGEABILITY OF VACCINES

There are no data available regarding interchangeability of the currently available Vero cell culture-derived JE vaccine (IXIARO®) with the previous mouse brain-derived JE vaccine, either in primary series or in booster dosing. Refer to Booster doses and re-immunization for additional information. Refer to Principles of Vaccine Interchangeability in Part 1 for additional general information.

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PART 4

MEASLES VACCINE

KEY INFORMATION (refer to text for details)

What	• Measles occurs worldwide and is one of the most highly communicable diseases. • Canada has imported cases and occasional outbreaks of measles. • Measles vaccine is available as measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) vaccine. • MMR vaccine or human immune globulin (Ig) may be used for measles post-exposure immunization in non-immune persons. • The efficacy of a single dose of measles vaccine given at 12 or 15 months of age is estimated to be 85% to 95%. With a second dose, efficacy is almost 100%. • Reactions to MMR and MMRV vaccine are generally mild and transient and include pain and redness at the injection site, low-grade fever and rash.
Who	• Measles-containing vaccine is recommended for routine immunization of children and for immunization of children and adolescents who missed measles immunization on the routine schedule. • Measles-containing vaccine is recommended for susceptible adults born in 1970 or later. • Adults born before 1970 can be presumed to have acquired natural immunity to measles; however, non-immune health care workers, travellers and military personnel should receive MMR vaccine, regardless of year of birth.
How	• **Routine childhood immunization:** administer two doses of measles-containing vaccine (MMR or MMRV); the first dose at 12 to 15 months of age and the second dose at 18 months of age or any time thereafter, but should be given not later than around school entry. • **Children and adolescents who are previously unimmunized:** administer two doses of measles-containing vaccine. The minimum interval between doses of MMR vaccine is 4 weeks. MMRV vaccine may be used in healthy children aged 12 months to 12 years. The recommended interval between 2 doses of MMRV vaccine is at least 3 months; a minimum interval of 6 weeks between doses may be used if rapid, complete protection is required. • **Susceptible adults born in 1970 or later:** administer one dose of MMR vaccine. Those who are at the greatest risk of measles exposure (travellers to destinations outside of North

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	America, health care workers, students in post-secondary educational settings, and military personnel) should receive two doses of MMR vaccine. • **Non-immune health care workers and military personnel born before 1970:** administer two doses of MMR vaccine at least 4 weeks apart • **Non-immune travellers born before 1970:** administer one dose of MMR vaccine. • **Non-immune students born before 1970:** consider administering one dose of MMR vaccine
Why	• Measles occurs worldwide and is one of the most highly communicable infectious diseases. • Complications of measles disease occur in about 10% of measles cases and death is estimated to occur in 1 to 2 of every 1,000 cases. • MMR and MMRV vaccines are safe and effective.

Since the publication of the *2006 Canadian Immunization Guide:*

- New recommendations have been made for measles vaccination of health care workers, travellers and military personnel.
- A new combined multivalent vaccine (measles-mumps-rubella-varicella vaccine [MMRV]) has become available for children aged 12 months to 12 years.

For additional information, refer to the National Advisory Committee on Immunization (NACI) Statements: Statement on Measles-Mumps-Rubella-Varicella Vaccine (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-9/index-eng.php) and Updated Recommendations for the use of Varicella and MMR Vaccines in HIV-infected Individuals. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-7/index-eng.php)

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Measles (rubeola, red measles) is caused by measles virus, a member of the *Paramyxoviridae* family.

Reservoir

Humans

Transmission

Measles is one of the most highly communicable infectious diseases with greater than 90% secondary attack rates among susceptible persons. The virus is transmitted by the airborne route, respiratory droplets, or direct contact with nasal or throat secretions of infected persons. The incubation period is about 10 days (range, 7 to 18 days). The interval from exposure to appearance of rash averages 14 days. Cases are infectious from 1 day before the beginning of the prodromal period to 4 days after rash onset. People who recover from measles have permanent immunity to the disease.

Risk factors

All persons who have not had measles disease or who have not been successfully vaccinated are at risk of infection. In Canada, adults born before 1970 are generally presumed to have acquired natural immunity to measles. Individuals at greatest risk of exposure to measles include travellers to destinations outside of North America, health care workers, students in post-secondary educational settings, and military personnel.

Seasonal/temporal patterns

Historically, measles disease occurs primarily in late winter and spring in temperate zones. It is now restricted to sporadic cases and outbreaks.

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Spectrum of clinical illness

Symptoms of measles include prodromal fever, cough, coryza, conjunctivitis, Koplik spots (white spots on the inner lining of the mouth) and a rash that typically begins on the face, advances to the trunk and then to the arms and legs. Complications such as otitis media and bronchopneumonia occur in about 10% of reported cases, even more commonly in those who are poorly nourished and chronically ill, and in infants less than 1 year of age. Measles encephalitis occurs in approximately 1 of every 1,000 reported cases and may result in permanent brain damage. Measles infection can cause subacute sclerosing panencephalitis (SSPE), a rare but fatal disease. In developed countries, death is estimated to occur in 1 to 2 of every 1,000 cases of measles. Measles during pregnancy results in a higher risk of premature labour, spontaneous abortion and low birth weight infants. Measles in an immunocompromised person may be severe.

DISEASE DISTRIBUTION

Incidence/prevalence

Global

Measles occurs worldwide and remains a serious and common disease in developing countries. According to the World Health Organization (WHO), measles is a leading cause of vaccine preventable deaths in children worldwide.

The global goal of reducing mortality due to measles by 90% by 2010 (compared with levels in 2000) was not reached. Measles was largely eliminated from the Western Hemisphere by 2002; however, in 2011 there were large measles outbreaks worldwide. There were over 26,000 cases in the WHO European Region with the highest number reported in France (more than 14,000 cases). Large outbreaks have also occurred in Africa, mostly in the Democratic Republic of the Congo, with more than 106,000 cases and 1,100 deaths.

National

Before the introduction of measles vaccine in 1963 to 1964, measles occurred in cycles with an increasing incidence every 2 to 5 years. At that time, an estimated 300,000 to 400,000 cases occurred annually. Since the introduction of vaccine, the incidence of measles has declined markedly in Canada (refer to *Figure 1*). Between 1989 and 1995, in spite of very high immunization coverage, there were many outbreaks involving predominately children who had received one dose of measles vaccine. It was estimated that 10% to 15% of immunized children remained unprotected after a single dose given at 12 months of age.

In 1996 to 1997, in an effort to reach the goal of measles elimination, every Canadian province and territory added a second dose of measles-containing vaccine to its routine immunization schedule, and most conducted catch-up programs in school-aged children with measles or measles-rubella vaccine. These interventions achieved immunization coverage for the second dose in excess of 85%, reducing the proportion of vulnerable children to a level that does not sustain endemic measles transmission. By 1998, endemic transmission of measles was interrupted.

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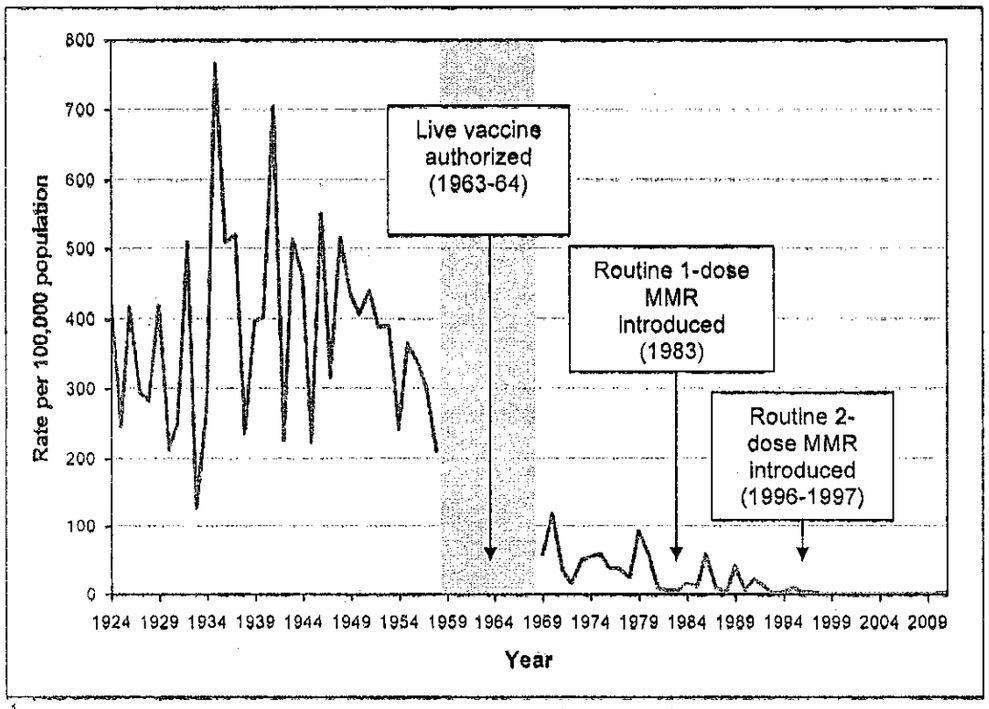
Figure 1: Reported incidence rate of confirmed measles cases, Canada 1924-2011[1]



[1] Measles was not nationally reportable between 1959 and 1968. The incidence rate for 2011 is annualized to August 31, 2011.

RECENT OUTBREAKS

Since the introduction of the two dose measles-containing vaccine schedule, outbreaks in Canada have been a result of importation from other countries.

In 2007, there was an outbreak in Quebec with 94 confirmed measles cases. The laboratory results suggested there were two separate importations. More than one-half of cases were between the ages of 1 and 10 years. Where immunization status was known, nearly all of the cases were individuals who had not received two doses of measles-containing vaccine.

In 2008, there was an outbreak in Ontario of 53 confirmed measles cases. About one-third of the cases were less than 10 years of age. Where immunization status was known, nearly all of the cases were not immunized.

In the spring of 2010, an outbreak in British Columbia resulted in 77 confirmed measles cases. Infants and children under 5 years of age were disproportionately affected, as were adults aged 30 to 39 years. Where immunization status was known, 59% of cases had not been vaccinated, 29% had received one dose of measles-containing vaccine and 12% had received two doses of measles-containing vaccine.

In Canada in 2011, measles importations led to a large outbreak involving more than 700 cases, largely in Quebec. The majority of the cases were between the ages of 10 and 19 years old. Where immunization status was known, approximately 80% of cases were not adequately immunized for their age.

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Refer to the Public health Agency of Canada Vaccine-Preventable Diseases webpage for the most recent information about the epidemiology of measles in Canada. (http://www.phac-aspc.gc.ca/im/vpd-mev/index-eng.php)

PREPARATIONS AVAILABLE FOR USE IN CANADA

MEASLES-CONTAINING VACCINES

- **M-M-R® II** (live, attenuated combined measles, mumps and rubella vaccine), Merck Canada Inc. (MMR)
- **PRIORIX®** (live, attenuated combined measles, mumps and rubella vaccine), GlaxoSmithKline Inc. (MMR)
- **PRIORIX-TETRA®** (live, attenuated combined measles, mumps, rubella and varicella vaccine), GlaxoSmithKline Inc. (MMRV)

In Canada, measles vaccine is only available in combination with mumps and rubella vaccine (MMR) or mumps, rubella and varicella vaccine (MMRV). In many countries outside of Canada measles vaccine alone is given.

HUMAN IMMUNE GLOBULIN

- **GamaSTAN® S/D** (immune globulin [human]), Grifols Therapeutics Inc. (Ig)

For complete prescribing information, consult the product leaflet or information contained within the product monograph available through Health Canada's Drug Product Database. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for lists of vaccines and passive immunizing agents available for use in Canada and their contents.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

The efficacy of a single dose of measles-containing vaccine given at 12 or 15 months of age is estimated to be 85% to 95%. With a second dose, efficacy in children approaches 100%. However, measles outbreaks have occurred in populations with high immunization coverage rates. Due to the high infectivity of measles (each case may infect 12 to 18 others) at least 95% of the population needs to be immunized to develop herd immunity. There are no data regarding the efficacy of MMRV vaccine.

IMMUNOGENICITY

In clinical studies a single injection of MMR vaccine induced measles antibodies in 95%, mumps antibodies in 96%, and rubella antibodies in 99% of previously seronegative children.

In a study of 12 month old children, a single dose of MMRV vaccine resulted in a seroconversion rate for measles, mumps, rubella and varicella of 98%, 97%, 98% and 93%, respectively. The seroconversion rates and geometric mean titres for individual components were not significantly different from those achieved after MMR plus univalent varicella vaccines or MMR vaccine alone. A study of children receiving two doses of MMRV vaccine during the second year of life noted seropositivity for measles, mumps, rubella and varicella of 99%, 97.4%, 100% and 99.4% respectively by the third year post-vaccination. Long-term persistence of anti-measles, anti-mumps, anti-rubella and anti-varicella antibodies following MMRV vaccinations are under evaluation.

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RECOMMENDATIONS FOR USE

CHILDREN (12 months to 17 years of age)

Two doses of measles-containing vaccine should be given for routine immunization of children and for immunization of children and adolescents who have missed measles immunization on the routine schedule. MMRV vaccine may be used in children aged 12 months to 12 years.
vaccine for varicella protection.

ADULTS (18 years of age and older)

Routine immunization: adults **born before 1970** are generally presumed to have acquired natural immunity to measles; however, some of these indivlduals may be susceptible.
Adults without contraindications, **born in 1970 or later** who do not have documented evidence of receiving measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles infection should be immunized with one dose of MMR vaccine.

Health care workers, regardless of their year of birth, who do not have documented evidence of receiving two doses of measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should receive two doses of MMR vaccine. Refer to Workers.

Students in post-secondary educational settings, **born in 1970 or later**, who do not have documented evidence of receiving two doses of measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should receive two doses of MMR vaccine. In students **born before 1970,** administration of one dose of MMR vaccine should be considered.

Military personnel, regardless of their year of birth, who do not have documented evidence of receiving two doses of measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should receive two doses of MMR vaccine.

Travellers to destinations outside of North America, **born in 1970 or later**, who do not have documented evidence of receiving two doses of measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should receive two doses of measles-containing vaccine. Travellers **born before 1970** who do not have documented evidence of receiving a measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should receive one dose of MMR vaccine. Refer to Travellers.

Table 1 provides a summary of criteria for measles immunity. Refer to *Schedule*.

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Table 1: Criteria for immunity to measles

Routine	Health care workers	Travellers to destinations outside North America	Students in post-secondary educational settings	Military personnel
Documentation of vaccination: • Children 12 months to 17 years of age: 2 doses[1] • Adults 18 years of age and older born in 1970 or later: 1 dose[1, 2] **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity **OR** Born before 1970	Documentation of vaccination with 2 doses[1] (regardless of year of birth) **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity	Documentation of vaccination: • If born in 1970 or later: 2 doses[1] • If born before 1970: 1 dose[1] **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity	Documentation of vaccination: • If born in 1970 or later: 2 doses[1] • If born before 1970: consider 1 dose[1] if no documentation of receipt of measles-containing vaccine **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity	Documentation of vaccination with 2 doses[1] (regardless of year of birth) **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity

1 Measles-containing vaccine
2 Refer to additional recommendations for health care workers, travellers to destinations outside of North America, students in post-secondary educational settings and military personnel.

PERSONS WITH INADEQUATE IMMUNIZATION RECORDS

Children and adults lacking adequate documentation of immunization should be considered unimmunized and started on an immunization schedule appropriate for their age and risk factors, unless known to be immune based on laboratory testing. MMR or MMRV vaccine, as appropriate, may be given regardless of possible previous receipt of the vaccine because additional adverse events associated with repeated immunization have not been demonstrated. Refer to Immunization of Persons with Inadequate Immunization Records in Part 3 for additional general information.

PREGNANCY AND BREASTFEEDING

Immunity to measles, mumps and rubella should be reviewed in women of reproductive age, and vaccination should be recommended to non-pregnant susceptible women. Ideally, the immunization status of women intending to become pregnant should be reviewed and vaccines updated as necessary prior to conception. Women should delay pregnancy by at least 28 days following vaccination with a live vaccine.

MMR and MMRV vaccines should generally not be given during pregnancy because of the theoretical risk of disease transmission to the fetus; however, there is no evidence demonstrating a teratogenic or other risk from such vaccines. There was no evidence of Congenital Rubella Syndrome in any of the offspring of 226 women inadvertently vaccinated during pregnancy. Inadvertent immunization with MMR vaccine is not a reason for pregnancy termination. In some situations, potential benefits of MMR vaccination may outweigh risks such as during measles or rubella outbreaks, in which case vaccination may be considered.

Women who are breastfeeding can be vaccinated with MMR vaccine.

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Refer to Contraindications, Precautions. Refer to Immunization in Pregnancy and Breastfeeding in Part 3 for additional general information.

IMMUNOCOMPROMISED PERSONS

In general, immunocompromised persons should not receive live vaccines because of the risk of disease caused by the vaccine strains. When considering immunization of an immunocompromised person with a live vaccine, **approval from the individual's attending physician should be obtained before vaccination.** For complex cases, referral to a consultant with expertise in immunization or immunodeficiency is advised.

Family or medical history

People who have a suspicious history for immunodeficiency disorders (e.g., known or suspected family history of congenital immunodeficiency disorder or HIV infection, or history of failure to thrive and recurrent infections) should not be immunized with a live vaccine until they have been fully investigated and T cell dysfunction ruled out. Immunodeficiency states may be undiagnosed in young children presenting for routine immunizations, which include live vaccines. This is particularly important to consider in infants receiving live vaccines before 12 months of age. A history of negative prenatal screening of the infant's mother for HIV should be obtained before administering a live vaccine. If a mother has not received routine prenatal care in Canada, the possibility of undiagnosed HIV infection should be considered.

Congenital (primary) immunodeficiency

Live vaccines are generally not recommended for people with congenital immunodeficiency states although some exceptions exist.

B cell deficiency

MMR vaccine, as appropriate for age, should be considered if the individual is not receiving regular immune globulin replacement therapy which may affect the efficacy of the vaccine.

T cell, natural killer T cell, and mixed cellular and antibody defects (e.g., Severe Combined Immune Deficiency [SCID])

All live vaccines, including MMR and MMRV, are contraindicated in people with defects in T cell function.

Phagocytic and neutrophil disorders (e.g., congenital neutropenia, leukocyte adhesion and migration defects, chronic granulomatous disease)

Children with phagocytic or neutrophil disorders may be vaccinated with MMR vaccine as appropriate for age.

Complement deficiency

There are no contraindications to the use of MMR vaccine in individuals with complement deficiency disorders. Immunity can decrease over time. Measurement of antibody titres and re-immunization, if needed, should be considered.

Acquired (secondary) immunodeficiency

Malignant hematologic disorders

MMR and MMRV vaccines are contraindicated in individuals with severe immunodeficiency due to blood dyscrasias, lymphomas, leukemias of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems and in people undergoing immunosuppressive treatment for malignancy. Children with Acute Lymphocytic Leukemia (ALL) may be vaccinated with MMR vaccine if the disease has been in remission for at least 12 months, the child's total lymphocyte

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count is at least 1.2 × 10^9/L, the child is not receiving radiation therapy, and maintenance chemotherapy can be withheld for at least 1 week before to 1 week after immunization.

Malignant solid tumours

MMR and MMRV vaccines are contraindicated in people undergoing immunosuppressive treatment for any malignant solid tumours.

Hematopoietic stem cell transplantation (HSCT- autologous or allogeneic)

- Pre-transplantation: People awaiting HSCT should not receive measles, mumps and rubella-containing vaccine. Vaccination of donors immediately before stem cell harvest is not recommended as there is no evidence that immunity can be transferred from the donor to the recipient and there are no safety data.
- Post-transplantation: Antibody titres to vaccine-preventable diseases decline after HSCT if the recipient is not re-vaccinated. Vaccination with MMR vaccine may be considered 24 months after transplantation provided there is no evidence of chronic graft-versus-host disease, immunosuppression has been discontinued for at least 3 months, and the person is considered immunocompetent by a transplant specialist. Serologic response should be checked after the first dose of MMR vaccine and a second dose should be given 3 months or more after the first dose if there is no seroconversion.

Solid organ transplantation

If possible, individuals being considered for solid organ transplantation should receive immunizations recommended for their age before the transplantation is performed. MMR vaccine may be given to infants as early as 6 months of age if transplantation is anticipated before 12 to 15 months of age. MMR vaccine should be given at least 4 weeks before solid organ transplantation and, in general, is not recommended after transplantation.

Immunosuppressive therapy

Vaccination status for measles, mumps and rubella should be reviewed for immunocompetent persons who might be anticipating initiation of immunosuppressive treatments or who have diseases that might lead to immunodeficiency. Refer to Immunization of Immunocompromised Persons in Part 3 for a list of immunosuppressive medications.

If indicated, MMR vaccine should be administered at least 4 weeks before the initiation of immunosuppressive therapy to reduce the risk of disease caused by the vaccine strain. If MMR vaccine cannot be given prior to initiation of immunosuppressive therapy, a period of at least 3 months should elapse after immunosuppressive drugs (except high-dose systemic corticosteroids) have been stopped before administration of live vaccines to reduce the risk of disease caused by the vaccine strain. A period of at least 4 weeks should elapse between discontinuation of high-dose systemic steroids and the administration of MMR vaccine. The interval between discontinuation of immunosuppressive drugs and MMR vaccine administration may vary with the intensity of the immunosuppressive therapy, underlying disease and other factors.

If immunosuppressive therapy cannot be stopped, live vaccines are generally contraindicated, although the risk-to-benefit ratio may favour immunization if only low doses of immunosuppressive drugs are required and there is significant risk of development of disease. The safety and efficacy of live, attenuated vaccines during low dose intermittent or maintenance therapy with immunosuppressive drugs (other than corticosteroids) are unknown. Immunosuppressive drugs have been reported to cause reactivation of latent tuberculosis infection and predisposition to other opportunistic infections. Therefore, until additional information becomes available, avoidance of MMR vaccines during intermittent or low dose chemotherapy or other immunosuppressive therapy is prudent.

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Corticosteroid therapy is not a contraindication to administering live vaccine when steroid therapy is short-term (i.e., less than 14 days); or a low-to-moderate dose (less than 2 mg/kg/day for a child or less than 20 mg/day of prednisone or its equivalent per day for an adult); or long-term, alternate-day treatment with short-acting preparations; or maintenance physiologic replacement therapy; or administered topically, inhaled, or locally injected (e.g., joint injection).

In general, live attenuated vaccines are contraindicated during monoclonal antibody treatment or in infants exposed to monoclonal antibodies. Monoclonal antibodies taken during pregnancy will be transferred to the fetus and their effects may persist after birth. Infants who have been exposed to monoclonal antibodies, either during pregnancy or from breastfeeding, should have B-cell enumeration. B cell enumeration should be normal before vaccination with live vaccines. Consultation with an immunologist is advised. Vaccination status should be reviewed prior to commencing monoclonal antibodies.

HIV-infected

An infectious disease specialist/immunologist should be consulted for advice on MMR immunization in HIV-infected people. There are no contraindications to the use of MMR vaccine early in the course of illness; however, MMR vaccine is contraindicated in persons with advanced HIV/AIDS. The safety and immunogenicity of MMRV vaccine in HIV-infected individuals has not been evaluated, and MMRV vaccine cannot be routinely recommended.

- Children: HIV-infected children 12 months of age and older, and with Centers for Disease Control and Prevention (CDC) clinical category N, A, or B and immunologic category 1 or 2 (i.e., CD4 counts ≥15%) may receive two doses of MMR vaccine 3 to 6 months apart. Univalent varicella vaccine may be administered concomitantly with MMR vaccine at different injection sites using separate needles and syringes.
- Adolescents and adults: immunization with two doses of MMR administered 3 months apart may be considered for susceptible HIV-infected adolescents and adults with CD4 cell count ≥200 x 10^6/L and CD4 percentage ≥15%.

Household contacts

Susceptible household contacts of immunocompromised people should receive a measles-containing vaccine as appropriate for age and risk factors.

Refer to Contraindications and Precautions. Refer to Immunization of Immunocompromised Persons in Part 3 for additional information.

PERSONS WITH CHRONIC DISEASES

Hyposplenism or asplenia

Hyposplenic or asplenic (congenital absence, surgical removal or functional [e.g., sickle cell disease]) individuals should be immune to measles, mumps and rubella or should receive MMR or MMRV vaccine as appropriate.

Chronic renal disease/dialysis

Individuals with chronic renal disease or undergoing dialysis should be immune to measles, mumps and rubella or should receive MMR or MMRV vaccine as appropriate.

Neurologic disorders

People with conditions such as autism spectrum disorders or demyelinating disorders (including multiple sclerosis) should receive all routinely recommended immunizations, including MMR or MMRV vaccine as appropriate.

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Autoimmune diseases

Individuals with autoimmune disease **not being treated with immunosuppressive drugs** are not considered significantly immunocompromised and should receive MMR immunization following consultation with their physician. Rheumatic disease modifying agents such as hydroxychloroquine, sulfasalazine, or auranofin are not generally identified as immunosuppressive.

Refer to Immunization of Persons with Chronic Diseases in Part 3 for additional general information.

TRAVELLERS

Protection against measles is especially important for people planning travel to destinations outside of North America. Travellers born in 1970 or later who do not have documented evidence of receiving two doses of measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should receive two doses of measles-containing vaccine.

Measles vaccine should be given at an earlier age than usual for children travelling to countries outside of North America. MMR vaccine may be given as early as 6 months of age; however, two additional doses of measles-containing vaccine must be administered after the child is 12 months old to ensure long lasting immunity to measles.

Travellers born before 1970, who do not have documented evidence of receiving measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should receive one dose of MMR vaccine.

Measles is endemic in many countries. Refer to measles incidence rates in WHO member countries for additional information. (http://www.who.int/immunization/monitoring_surveillance/en/)

Refer to Immunization of Travellers in Part 3 for additional general information

PERSONS NEW TO CANADA

Health care providers who see persons newly arrived in Canada should review the immunization status and update immunization for these individuals. In many countries outside of Canada, mumps and rubella vaccines are in limited use and measles vaccine alone is given. A Canadian study showed that more than one-third of new immigrants and refugees, particularly women, were susceptible to measles, mumps, or rubella. Refer to Immunization of Persons New to Canada in Part 3 for additional general information.

WORKERS

It is recommended that all health care workers be immune to measles. Health care workers, regardless of their year of birth, who do not have documented evidence of receiving two doses of measles-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed measles disease should be vaccinated accordingly so that they have received two doses of MMR vaccine.

POST-EXPOSURE IMMUNIZATION

Measles may continue to be imported into Canada. Outbreaks may occur in susceptible populations. For practical purposes, all individuals attending the same school or facility should be considered contacts.

MMR vaccine

Susceptible, immunocompetent individuals 12 months of age and older who are exposed to measles may be protected from measles disease if they are given MMR vaccine within 72 hours of their exposure. MMR vaccine may be recommended for children between 6 months to less than 12 months of age for post-exposure management if it is given within 72 hours of exposure; however, two additional doses of measles-containing vaccine must be administered after the child is 12 months old (and at least 28 days from the previous dose) to ensure long lasting immunity to measle

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Human immune globulin (Ig)

Prophylactic use of Ig has been shown to be effective in modifying or preventing disease if administered within 6 days after exposure to measles, however, it should be given as soon as possible after exposure when indicated. Ig should be considered for contacts of measles who are:

1. susceptible pregnant women,
2. susceptible immunocompromised people, or
3. children less than 6 months of age.

Measles-containing vaccine is contraindicated in groups 1 and 2 and effectiveness and safety has not been established in group 3. Ig should also be considered for susceptible immunocompetent contacts of measles who are 6 months of age and older and who present more than 72 hours after exposure (when MMR vaccine no longer provides post-exposure protection) but within 6 days after exposure (when Ig may still provide post-exposure protection).

In HIV infected individuals, measles antibody titre is known to decline more rapidly over time as compared to those who are HIV uninfected. A dose of Ig should be considered in HIV infected individuals with severe immunosuppression after a known exposure to confirmed measles, even with documented previous MMR immunization. Regardless of vaccination status pre-transplant, Ig should also be considered for hematopoietic stem cell transplantation (HSCT) recipients, unless vaccinated post HSCT and known to have an adequate measles antibody titre.

In assessing the extent of measles exposure and deciding between MMR vaccine and Ig for post-exposure management, it is important to consider that Ig only provides short-term protection and requires postponing the administration of MMR vaccine for 5 to 6 months. If longer- term protection against measles is required because of ongoing measles transmission in the community, MMR vaccine may be the preferred choice. It is important to note that despite the use of MMR vaccine or Ig for post-exposure management, measles infection may still occur. Exposed individuals should be counseled regarding signs and symptoms of measles; counseling should include avoiding contact with others should they become ill with symptoms compatible with measles and the need to seek medical care, including advising health care workers of the possibility of measles before going to a health care setting so that appropriate precautions can be taken. For detailed information regarding infection prevention and control, refer to the Guidelines for the Prevention and Control of Measles Outbreaks in Canada. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-3/index-eng.php)

The recommended dose of Ig for healthy individuals exposed to measles is 0.25 mL/kg of body weight given by the IM route. The dose for exposed individuals who are immunocompromised is 0.5 mL/kg of body weight. A maximum dose of 15 mL should not be exceeded. For complete prescribing information, consult the product leaflet or information contained within the product monograph available through Health Canada's Drug Product Database. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php)

Individuals receiving replacement IVIg (400 mg/kg of body weight or higher) are considered protected and do not require Ig if the last dose of IVIg was received within the three weeks prior to measles exposure.

Unless it is contraindicated, individuals who receive Ig should receive measles-containing vaccine after specified intervals, once the measles antibodies administered passively have degraded. For recommendations on the interval between administration of an Ig preparation or blood product and vaccination with measles-containing vaccine, refer to Blood Products, Human Immune Globulin and Timing of Immunization in Part 1.

Refer to Passive Immunizing Agents in Part 5 for additional general information.

OUTBREAK CONTROL

Immunization with MMR vaccine is an integral element of a comprehensive measles outbreak prevention and management strategy. In a measles outbreak, MMR vaccine can be provided at any time starting from 6 months of age. However if given between 6 months and less than 12 months of age, two additional doses of measles-containing vaccine must be administered after the child is 12 months old (and at least 28 days from the previous dose) to ensure long lasting immunity to measles. For detailed information on outbreak control, refer to the Guidelines for the Prevention and Control of Measles Outbreaks in Canada. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-3/index-eng.php)

VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

Dose

Each dose is 0.5 mL.

Route of administration

MMR vaccine should be administered subcutaneously; MMRV can be administered subcutaneously or intramuscularly. Refer to Vaccine Administration Practices in Part 1 for additional information.

Schedule

Children (12 months to 12 years of age)

For routine immunization of children aged 12 months to 12 years, two doses of measles-containing vaccine (MMR or MMRV) should be administered. The first dose of measles-containing vaccine should be administered at 12 to 15 months of age and the second dose at 18 months of age or any time thereafter, but should be given no later than around school entry.

The recommended minimum interval between doses of MMR vaccine is 4 weeks. Children who previously received a single dose of MMR vaccine should receive a second dose at least 4 weeks after the first dose. The recommended interval between two doses of MMRV vaccine is at least 3 months; a minimum interval of 6 weeks between doses may be used if rapid, complete protection is required.

Adolescents (13 to 17 years of age)

Measles-susceptible adolescents should receive two doses of MMR vaccine given at least 4 weeks apart.

Adults (18 years of age and older)

Measles-susceptible adults should receive one or two doses of MMR vaccine as appropriate for age and risk factors (refer to *Table 1*). If two doses are needed, MMR vaccine should be administered with a minimum interval of 4 weeks between doses.

BOOSTER DOSES AND RE-IMMUNIZATION

Re-immunization with measles-containing vaccine after age and risk appropriate vaccination is not necessary.

SEROLOGICAL TESTING

Serological testing may be indicated to confirm the diagnosis of measles or to determine immune status. Serologic testing is not recommended before or after receiving measles-containing vaccine. If serology is inadvertently done subsequent to appropriate measles immunization and does not demonstrate immunity, measles re-immunization is not necessary.

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STORAGE REQUIREMENTS

M-M-R® II: Maintain vaccine at +10°C or colder during shipment. Freezing during shipment will not affect potency of the vaccine. Protect the vaccine from light. Before reconstitution, store the vial of vaccine at +2°C to +8°C or colder. The diluent may be stored in the refrigerator or at room temperature and must not be frozen.

PRIORIX®: Store in a refrigerator at +2°C to +8°C. The diluent may be stored separately at room temperature. Protect from light.

PRIORIX-TETRA®: Store the vaccine and diluent in a refrigerator at +2°C to +8°C and do not freeze. Protect the vaccine from light.

Refer to Storage and Handling of Immunizing Agents in Part 1 for additional general information. Refer to Passive Immunizing Agents Part 5 for information regarding Ig storage requirements.

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

Live vaccines given by the parenteral route may be administered concomitantly with all other vaccines during the same visit using different injection sites and separate needles and syringes. In general, if two live parenteral vaccines are not administered concomitantly, there should be a period of at least 4 weeks before the second live parenteral vaccine is given. Exceptions are varicella-containing vaccines, such as MMRV vaccine:

- administer doses of varicella-containing vaccine at least 3 months apart for children 1 to 12 years of age. If rapid, complete protection against varicella is required, a minimum interval of 6 weeks between 2 doses may be used for children 1 to 12 years of age.
- do not concomitantly administer varicella-containing vaccines with smallpox vaccine; administer varicella-containing vaccine and smallpox vaccine at least 4 weeks apart.

Oral and intranasal vaccines can be given at the same time as, or any time before or after any other live vaccine, regardless of the route of administration of the other live vaccine.

Refer to Timing of Vaccine Administration in Part 1 for additional general information.

VACCINE AND IMMUNE GLOBULIN SAFETY AND ADVERSE EVENTS

Refer to Vaccine Safety Part 2 for additional general information.

COMMON AND LOCAL ADVERSE EVENTS

MMR vaccine

Adverse events following MMR immunization occur less frequently and are less severe than those associated with natural disease. Adverse reactions are less frequent after the second dose of vaccine and tend to occur only in those not protected by the first dose. Six to 23 days after MMR immunization, approximately 5% of immunized children experience malaise and fever (with or without rash) lasting up to 3 days. Parotitis, rash, lymphadenopathy, and joint symptoms also occur occasionally after MMR immunization.

MMRV vaccine

Pain and redness at the injection site or low-grade fever occur in 10% or more of vaccinees. Rash, including measles-like, rubella-like and varicella-like rash, as well as swelling at the injection site and moderate fever (greater than 39°C) occur in 1% to less than 10% of vaccinees. As varicella-like rashes that occur within the first two weeks after immunization may be caused by wild-type virus, health care

providers should obtain specimens using viral transport media from a lesion to ensure varicella disease is not confused with a reaction to vaccination.

Rubella-containing vaccines

Acute transient arthritis or arthralgia may occur 1 to 3 weeks after immunization with rubella-containing vaccine, lasts for about 1 to 3 weeks, and rarely recurs. This is more common in post-pubertal females, among whom arthralgia develops in 25% and arthritis in 10% after immunization with rubella-containing vaccine. There is no evidence of increased risk of new onset, chronic arthropathies or neurologic conditions.

Ig

Injection site pain and tenderness, urticaria, and angioedema may occur.

LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

MMR and MMRV vaccines

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. As with other vaccines, anaphylaxis following vaccination with MMR or MMRV vaccine may occur but is very rare.

Immune Thrombocytopenic Purpura (ITP)

Rarely, ITP occurs within 6 weeks after immunization with MMR or MMRV vaccine. In most children, post-immunization thrombocytopenia resolves within three months without serious complications. In individuals who experienced ITP with the first dose of MMR or MMRV, serologic status may be evaluated to determine whether an additional dose of vaccine is needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases.

Encephalitis

Encephalitis has been reported in association with administration of measles vaccine in approximately 1 per million doses distributed in North America which is much lower than that observed with natural measles disease (1 per 1,000 cases).

Febrile seizures

Recent studies have found a higher risk of febrile seizures with the first dose of a MMRV vaccine (ProQuad®, not authorized for use in Canada) when compared to the concomitant administration of MMR and univalent varicella vaccine. Data from the United States (US) estimated that the risk of febrile seizures in the 5 to 12 days following the first dose of this MMRV vaccine is 1 for every 2,600 vaccinated children aged 12 to 23 months. Experience with the MMRV vaccine available in Canada is more limited; however, one study showed an additional risk of febrile seizures with MMRV vaccine compared to MMR and univalent varicella vaccines given as two separate products administered concomitantly. The risk with the Canadian vaccine was smaller than the risk found with the US product. Close surveillance and further investigation are underway.

Ig

Anaphylactic reactions, although rare, have been reported following the injection of human immune globulin.

OTHER REPORTED ADVERSE EVENTS AND CONDITIONS

In the mid to late 1990s, researchers from the United Kingdom reported an association between MMR vaccine and inflammatory bowel disease, and MMR vaccine and autism. Rigorous scientific studies and reviews of the evidence have been done worldwide, and there is now considerable evidence to refute

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those claims. In 2010, the original study suggesting a link between the MMR vaccine and autism was found to be fraudulent and was retracted.

GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Vaccine providers are asked to report the following AEFI in particular, through local public health officials:

- Febrile seizures within 30 days after vaccination with MMR or MMRV vaccine,
- Varicella that is moderate (50 to 500 lesions) or severe (more than 500 vesicular lesions or associated complications or hospital admission) and occurs 7 to 21 days after vaccination with MMRV vaccine,
- Any serious or unexpected adverse event felt to be temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI.

Refer to Reporting Adverse Events Following Immunization (AEFI) in Canada (http://www.phac-aspc.gc.ca/im/aefi-essi_guide/index-eng.php) and Vaccine Safety in Part 2 for additional information about AEFI reporting.

CONTRAINDICATIONS AND PRECAUTIONS

MMR and MMRV vaccines and Ig are contraindicated in persons with a history of anaphylaxis after previous administration of the product and in persons with proven immediate or anaphylactic hypersensitivity to any component of the product (with the exception of egg allergy for MMR and MMRV vaccines [refer below]), or its container. Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for lists of vaccines and passive immunizing agents available for use in Canada and their contents. For measles-containing vaccines, potential allergens include:

- M-M-R®II: neomycin, phenol red, porcine gelatin, residual components of chick embryo cell cultures
- PRIORIX®: egg protein, neomycin
- PRIORIX-TETRA®: egg protein, neomycin

In situations of suspected hypersensitivity or non-anaphylactic allergy to vaccine components, investigation is indicated which may involve immunization in a controlled setting. Consultation with an allergist is advised.

The measles and mumps components of MMR and MMRV vaccines are produced in chick embryo cell culture and may contain traces of residual egg protein. The trace amount of egg protein in the vaccine appears to be insufficient to cause an allergic reaction in egg-allergic individuals. Prior egg ingestion is not a prerequisite for immunization with egg protein-containing vaccine. Skin testing is not recommended prior to vaccination as it does not predict reaction to the vaccine. MMR or MMRV vaccine can be administered in the routine manner to people who have a history of anaphylactic hypersensitivity to hens' eggs. For all vaccines, immunization should always be performed by personnel with the capability and facilities to manage adverse events post-vaccination. Refer to Anaphylactic Hypersensitivity to Egg and Egg-Related Antigens in Part 2 for additional information.

Children with a known or suspected family history of congenital or hereditary immunodeficiency that is a contraindication to vaccination with live vaccine should not receive live vaccines unless their immune competence has been established.

MMRV vaccine is contraindicated in persons with impaired immune function, including primary or secondary immunodeficiency disorders. Refer to Immunocompromised persons.

MMR and MMRV vaccines are contraindicated during pregnancy. Refer to Pregnancy and breastfeeding.

MMR vaccine is contraindicated in individuals with active, untreated tuberculosis. While tuberculosis may be exacerbated by natural measles infection, there is no evidence that measles-containing vaccines, such

as MMR or MMRV have such an effect.

A history of febrile seizures or a family history of convulsions is not a contraindication for the use of MMRV vaccine.

Administration of MMR or MMRV vaccine should be postponed in persons with severe acute illness. Persons with a minor acute illness (with or without fever) may be vaccinated.

It is recommended to avoid the use of salicylates (e.g., acetylsalicylic acid [ASA]) for 6 weeks after immunization with MMRV vaccine because of an association between wild-type varicella, salicylate therapy and Reye's syndrome.

Refer to Contraindications, Precautions and Concerns in Part 2 and Passive Immunizing Agents Part 5 for additional general information.

DRUG INTERACTIONS

Systemic antiviral therapy (such as acyclovir, valacyclovir, famciclovir) should be avoided in the peri-immunization period, as it may reduce the efficacy of varicella-containing vaccine such as MMRV. On the basis of expert opinion, it is recommended that people taking long-term antiviral therapy should discontinue these drugs, if possible, from at least 24 hours before administration of MMRV vaccine and should not restart antiviral therapy until 14 days after.

The measles component in measles-containing vaccines can temporarily suppress tuberculin reactivity, resulting in false-negative results. If tuberculin skin testing or an Interferon Gamma Release Assay (IGRA) test is required, it should be done on the same day as immunization or delayed for at least 4 weeks after measles vaccination. Vaccination with measles-containing vaccine may take place at any time after tuberculin skin testing has been performed and/or read.

Passive immunization with human Ig or receipt of most blood products can interfere with the immune response to MMR and MMRV vaccines. These vaccines should be given at least 14 days prior to administration of an Ig preparation or blood product, or delayed until the antibodies in the Ig preparation or blood product have degraded. If the interval between administration of vaccine and subsequent administration of an Ig preparation or blood product is less than 14 days, the vaccine dose should be repeated after the recommended interval. The recommended interval between administration of an Ig preparation or blood product and subsequent immunization varies, depending on the Ig preparation or blood product. If the vaccine is given too early following Ig or blood product administration, it should be repeated after the appropriate interval has passed. Palivizumab (RSVAb) and washed red blood cell transfusion do not interfere with the antibody response to MMR or MMRV vaccines. Refer to Blood Products, Human Immune Globulin and Timing of Immunization in Part 1 for additional general information.

OTHER CONSIDERATIONS

INTERCHANGEABILITY OF VACCINES

On the basis of expert opinion, the MMR vaccines authorized in Canada may be used interchangeably. Refer to Principles of Vaccine Interchangeability in Part 1 for additional general information.

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PART 4

MENINGOCOCCAL VACCIN

KEY INFORMATION (refer to text for details)

What	• Almost all invasive meningococcal disease (IMD) is associated with *Neisseria meningitidis* serogroups A, B, C, Y, and W-135. • Worldwide, IMD occurs sporadically and in focal epidemics. IMD is endemic in Canada but occurs at low rates. • In Canada, the incidence of IMD is highest in infants and most cases are serogroup B for which there is no vaccine. • Persons at higher risk of IMD include: o persons with functional or anatomic asplenia o persons with congenital complement, properdin, factor D or primary antibody deficiencies o persons with acquired complement deficiencies (e.g., those receiving eculizumab (Soliris™) o travellers to areas with high rates of endemic meningococcal infection or transmission, including travellers to the meningitis belt of sub-Saharan Africa and pilgrims to the Hajj in Mecca, Saudi Arabia o research, industrial and clinical laboratory personnel who are potentially routinely exposed to *N. meningitidis* o military personnel who are at increased risk of meningococcal disease o HIV positive individuals should be considered for vaccination, especially if HIV is congentially acquired • Meningococcal vaccines are initially highly effective; effectiveness wanes over time. • Monovalent conjugate meningococcal vaccine (Men-C-C) effectiveness in infants is 97% within one year of vaccination. Vaccine effectiveness of the quadrivalent conjugate meningococcal vaccine Menactra® in adolescents is 80% to 85% within 3 to 4 years of vaccination. • There may be redness, swelling and soreness at the injection site.

Who	• **Healthy children:** should be immunized with a Men-C-C vaccine routinely at 12 months of age; however, they may begin meningococcal immunization earlier depending on provincial/territorial schedules. If not previously immunized as infants or toddlers Men-C-C vaccine should be given to children less than 5 years of age and considered for children 5 to 11 years of age. • **Adolescents and young adults:** either a Men-C-C or a quadrivalent conjugate meningococcal (Men-C-ACYW-135) vaccine (depending on local epidemiology and programmatic considerations) is recommended for adolescents (routinely at 12 years of age) and young adults even if previously vaccinated as an infant or toddler. • **High risk individuals**: Men-C-ACYW-135 vaccine is recommended for children and adults with increased risk of IMD. The choice of vaccine and recommended schedule vary with age. Periodic booster doses are recommended. • **Post-exposure management:** chemoprophylaxis is recommended for close contacts. If the serogroup is vaccine-preventable, immunoprophylaxis should also be considered depending on the exposure history. Recommendations for immunoprophylaxis in those previously vaccinated are provided.
How	• **Routine infant immunization:** give Men-C-C vaccine to healthy infants according to provincial/territorial schedules. • **12 months to 11 years of age:** give one dose of Men-C-C vaccine at 12 to 23 months of age (routinely at 12 months) whether immunized as an infant or not. For previously unimmunized children less than 5 years of age, give one dose of Men-C-C vaccine. Consider one dose of Men-C-C vaccine in children aged 5 to 11 years who were previously unimmunized. • **12 to 24 years of age**: give adolescents (routinely at 12 years of age) and young adults one dose of either Men-C-C or Men-C-ACYW-135 vaccine, even if previously vaccinated as an infant or toddler. • Men-C-C vaccine may be administered concomitantly with routine childhood vaccines and Men-C-ACYW-135 vaccine may be administered concomitantly with adolescent and adult age-appropriate vaccines at different injection sites using separate needles and syringes. • Menveo™ can be administered with routine paediatric vaccines; however, further studies are needed with regard to concomitant administration with pneumococcal 13-valent conjugate vaccine.
Why	• IMD mortality is approximately 10%. • Of IMD survivors, 10% to 20% have long term sequelae which include hearing loss, neurologic disabilities, and digit or limb amputations.

Since the publication of the 2006 *Canadian Immunization Guide:*

- Two new quadrivalent conjugate meningococcal vaccines for serogroups A, C, Y, and W-135 have become available.
- Bivalent polysaccharide meningococcal vaccine is no longer available in Canada.
- Recommendations for routine vaccination have been modified.
- Schedules (including booster doses) have been revised for high risk individuals as has the list of high risk individuals.
- Recommendations for post-exposure immunoprophylaxis of close contacts of IMD who have been previously immunized have been provided.

For additional information, refer to the National Advisory Committee on Immunization (NACI) *Statement/Update on the Use of Quadrivalent Conjugate Meningococcal Vaccines*. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/acs-dcc-3/index-eng.php)

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EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Meningococcal disease is caused by an aerobic encapsulated diplococcus, *Neisseria meningitidis* (meningococcus). Meningococcal serogroups are classified according to the immunologic reactivity of the polysaccharide capsule. Almost all invasive meningococcal disease (IMD) is associated with serogroups A, B, C, Y, and W-135. Meningococcal serogroups A, B, and C cause the majority of disease worldwide and are responsible for most sporadic cases and outbreaks.

Reservoir

Humans are the only reservoir for *N. meningitidis*.

Transmission

Meningococci are transmitted person-to-person by mucosal contact with respiratory droplets from the nose and throat of infected persons. Most people who are colonized with meningococci are asymptomatic carriers. Meningococcal disease is characterized by a short incubation period (2 to 10 days, usually 3 to 4 days).

Risk factors

Risk factors for the development of IMD include: complement, properdin or factor D deficiencies; functional or anatomic asplenia (including sickle cell disease); certain genetic risk factors; household exposure to an infected person; concurrent respiratory tract infection; recent influenza; household crowding; and active and passive smoking. Persons with HIV infection may be at increased risk for meningococcal disease; especially if HIV is congenitally acquired.

Seasonal/temporal patterns

Although disease occurs year-round, there is seasonal variation with the majority of cases occurring in the winter-spring period in temperate climates and in the dry season in tropical climates. Most noteworthy is the "meningitis belt" of sub-Saharan Africa where the majority of cases occur from December to June. For further information, refer to the Committee to Advise on Tropical Medicine and Travel (CATMAT) website: about CATMAT. (http://www.phac-aspc.gc.ca/tmp-pmv/catmat-ccmtmv/index-eng.php)

Spectrum of clinical illness

Invasive meningococcal disease usually presents as an acute febrile illness with rapid onset and features of meningitis or septicemia (meningococcemia), or both, and a characteristic non-blanching petechial or purpuric rash. Symptoms of meningococcal meningitis include intense headache, fever, nausea, vomiting, photophobia and stiff neck. Meningococcemia is characterized by circulatory collapse, haemorrhagic skin rash and a high fatality rate. Overall mortality is approximately 10%, and 10% to 20% of survivors have long term sequelae which include hearing loss, neurologic disabilities, and digit or limb amputations.

DISEASE DISTRIBUTION

Incidence/prevalence

Global

Invasive meningococcal disease occurs sporadically worldwide and in focal epidemics. The traditional endemic areas of the world include the savannah areas of sub-Saharan Africa (known as the meningitis belt) extending from Gambia and Senegal in the west to Ethiopia and Western Eritrea in the east. Serogroup A disease predominates in Africa and Asia, while serogroup B

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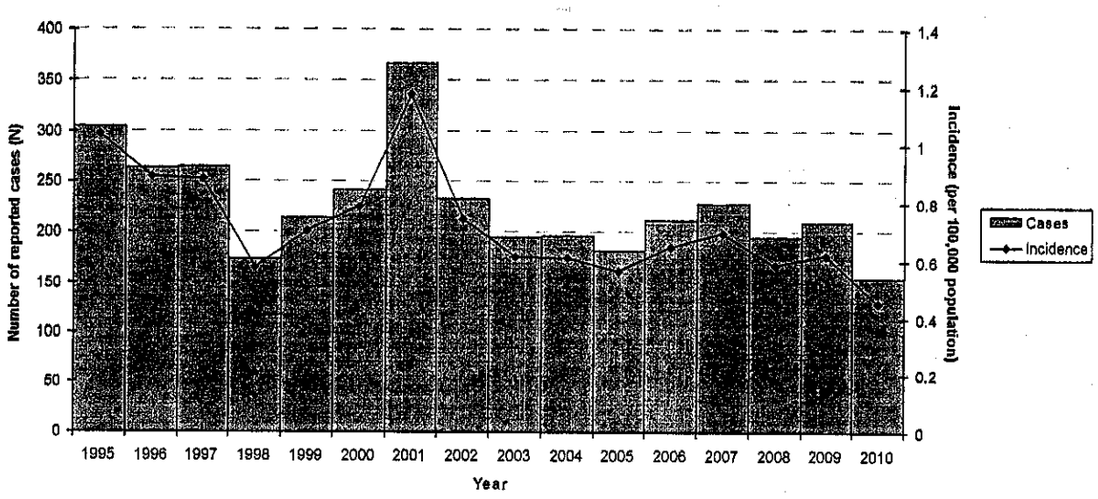
disease is predominant in Europe and most of the Americas. Meningococcal disease is also associated with the Hajj, an Islamic pilgrimage to Mecca, Saudi Arabia.

National

Invasive meningococcal disease is endemic in Canada, but rare. From 1985 to 2010, the overall incidence of IMD ranged between 0.4 to 1.6 cases per 100,000 population (refer to *Figure 1*). Incidence peaked in 1990 and again in 2001 due to localized outbreaks of serogroup C disease. Immunization campaigns using meningococcal serogroup C polysaccharide and conjugate vaccines were implemented in some regions during outbreaks from 1999 to 2001. Between 2002 and 2007, all Canadian provinces and territories implemented routine vaccination programs at various ages with monovalent meningococcal (serogroup C) conjugate vaccine, and since 2007 some have implemented routine adolescent quadrivalent meningococcal (serogroups A, C, Y, W-135) conjugate vaccination programs.

From 2005 to 2010, an average of 197 cases of IMD was reported annually in Canada, with an average incidence of 0.60 cases per 100,000 population. During this time period, incidence rates were highest among infants less than one year of age (average 7 cases per 100,000), followed by 1 to 4 year olds (1.81), and 15 to 19 year olds (1.18). As seen in *Figure 2*, the majority of cases with serogroup information from 2005 to 2010 were due to serogroup B (59%), which is not preventable by current vaccines. Serogroup C incidence has fallen dramatically to the extent that in 2010 its incidence fell to a level similar to that of serogroup W-135. Serogroup Y replaced C as the second most frequent serogroup by 2007. Cases caused by other serogroups were rare. The average number of cases caused by serogroups B, C, Y, and W-135 reported annually from 2005 to 2010 were 110, 29, 31, and 11, respectively. From 2005 to 2010, 6.7% of reported cases died. Case fatality ratios differed by serogroup, with serogroup C having the highest at 13% and serogroups B and W-135 having the lowest at around 4%.

Figure 1: Reported cases and incidence (per 100,000) of invasive meningococcal disease in Canada, 1995 to 2010*



* Case data obtained from the National Enhanced Invasive Meningococcal Disease Surveillance System. Data for 2007 to 2010 are preliminary. Population data obtained from Statistics Canada annual estimates.

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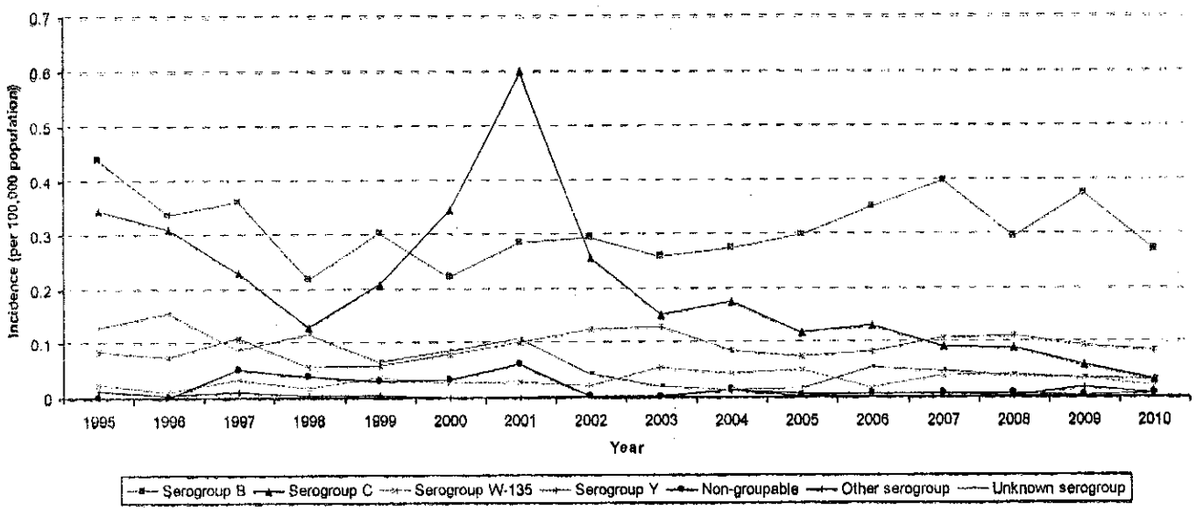
Figure 2: Incidence of invasive meningococcal disease per 100,000 population in Canada by serogroup and year, 1995 to 2010*



* Case data obtained from the National Enhanced Invasive Meningococcal Disease Surveillance System. Data for 2007 to 2010 are preliminary. Population data obtained from Statistics Canada annual estimates.

RECENT OUTBREAKS

Current meningococcal disease outbreak information is available from the World Health Organization (WHO) at: Global Alert and Response (GAR) Meningococcal Disease. (http://www.who.int/csr/don/archive/disease/meningococcal_disease/en/)

PREPARATIONS AUTHORIZED FOR USE IN CANADA

MENINGOCOCCAL VACCINES

Monovalent conjugate meningococcal vaccines (Men-C-C)

- **Meningitec®** (meningococcal group C oligosaccharides conjugated to CRM_{197} protein), Berna Biotech, AG (manufacturer), Pfizer Canada Inc. (distributor). (Men-C-C)
- **Menjugate®** (meningococcal group C oligosaccharide conjugated to CRM_{197} protein), Novartis Vaccines and Diagnostics (sponsor), Novartis Pharmaceuticals Canada Ltd. (distributor). (Men-C-C)
- **NeisVac-C®** (meningococcal group C polysaccharide conjugated to tetanus toxoids), Baxter (manufacturer), GlaxoSmithKline Inc. (distributor). (Men-C-C)

Quadrivalent conjugate meningococcal vaccines (Men-C-ACYW-135)

- **Menactra®** (meningococcal groups A, C, Y, and W-135 polysaccharides conjugated to diphtheria toxoid protein), sanofi pasteur Ltd. (Men-C-ACYW-135)
- **Menveo™** (meningococcal groups A, C, Y and W-135 oligosaccharide conjugated to CRM_{197} protein), Novartis Vaccines and Diagnostics Inc. (Men-C-ACYW-135)

Quadrivalent polysaccharide meningococcal vaccine (Men-P-ACYW-135)

- **MENOMUNE® A/C/Y/W-135** (meningococcal groups A, C, Y and W-135 polysaccharide antigens), Sanofi Pasteur Inc. (manufacturer), sanofi pasteur Ltd. (distributor). (Men-P-ACYW-135). Polysaccharide meningococcal vaccine is available in Canada but its use is not routinely recommended.

Vaccines against meningococcal serogroup B disease are under development.

For complete prescribing information, consult the product leaflet or information contained within Health Canada's authorized product monographs available through the *Drug Product Database*. (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Refer to *Table 1* in *Contents of Immunizing Agents Available for Use in Canada* in Part 1 for a list of all vaccines available for use in Canada and their contents.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

A study of Men-C-C vaccine demonstrated effectiveness in infants of 97% within one year of vaccination, decreasing to 68% after 1 year. Longer term vaccine effectiveness requires receipt of a booster dose in the second year of life for those immunized in infancy. Vaccine effectiveness of Menactra® within 3 to 4 years of vaccination in adolescence is 80% to 85%; however, effectiveness wanes over time. There is no efficacy or effectiveness data available for Menveo™. Vaccine effectiveness measured at individual level may under-estimate the impact of the program on meningococcal disease burden in the community due to the additional benefit conferred by herd immunity.

IMMUNOGENICITY

Men-C-C and Men-C-ACYW-135 vaccines are immunogenic in infants and toddlers but those vaccinated in infancy show a waning immune response. Vaccination with conjugate meningococcal vaccine primes the immune system for memory and induces good anamnestic responses; however, anamnestic response may not be sufficient to prevent disease after exposure and circulating antibodies are thought to be essential. In comparison to polysaccharide meningococcal vaccine, conjugate meningococcal vaccines demonstrate greater immunogenicity and induce better immunologic memory. Conjugate meningococcal vaccines do not result in hyporesponsiveness and have been shown to overcome the hyporesponsiveness evident with polysaccharide meningococcal vaccine usage.

RECOMMENDATIONS FOR USE

HEALTHY INFANTS AND CHILDREN (2 months to 11 years of age)

Infants may receive Men-C-C vaccine beginning at 2 months of age depending on the provincial/territorial schedule and the incidence of meningococcal serogroup C disease in their jurisdiction. Men-C-C vaccine is recommended for all children at 12 to 23 months of age regardless of any doses given at less than 12 months of age. It is routinely given at 12 months and is recommended in unimmunized children less than 5 years of age. Men-C-C vaccine may be considered for children 5 to 11 years of age if not previously immunized as infants or toddlers.

HEALTH ADOLESCENTS AND YOUR ADULTS (12 to 24 years of age)

Either Men-C-C or Men-C-ACYW-135 vaccine (depending on local epidemiology and programmatic considerations) is recommended for adolescents (routinely at 12 years of age) and young adults, even if previously vaccinated as an infant or toddler.

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HIGH RISK GROUPS

Underlying medical conditions

Individuals with increased risk of meningococcal disease because of underlying medical conditions are as follows:

- persons with functional or anatomic asplenia (including sickle cell disease)
- persons with congenital complement, properdin, factor D or primary antibody deficiencies
- persons with acquired complement deficiency due to receipt of the terminal complement inhibitor eculizumab (Soliris™)
- Men-C-ACYW-135 vaccine should be considered for individuals with HIV, especially if congenitally acquired.

Table 3 outlines the recommended schedule for vaccination of individuals who are at high risk due to underlying medical conditions. For those 1 year of age or older, two doses of Men-C-ACYW-135 vaccine, 8 weeks apart, are recommended.

There is limited evidence on the need for boosters. Based on expert opinion and the evidence to date, a booster dose for individuals in high risk groups is recommended every 3 to 5 years if vaccinated at 6 years of age and younger, and every 5 years for those vaccinated at 7 years of age and older. If a one dose primary series was used, give the second dose at the next available opportunity and then begin the booster doses based on the above intervals after the second dose.

Increased risk of exposure

Men-C-ACYW-135 vaccine is recommended for individuals at increased risk of exposure to meningococcal disease as follows:

- travellers (2 years of age and older) when meningococcal vaccine is recommended or required, including travellers to sub-Saharan Africa and pilgrims to the Hajj in Mecca, Saudi Arabia. Refer to *Table 1* for recommendations for travellers 2 to 23 months of age.
- laboratory personnel who are potentially routinely exposed to *N. meningitidis*
- military personnel during recruit training and on certain deployments

A booster dose is recommended every 5 years if individuals in these groups remain at ongoing risk (every 3 to 5 years in children vaccinated at 6 years of age or younger). Refer to *Travellers* or *Workers* sections for additional information.

Meningococcal vaccine is also recommended for most close contacts of a case of IMD and for outbreak control, if the disease is caused by a serogroup contained in the vaccine. Refer to *Post-exposure management* and *Outbreak control* for additional information.

Age considerations for choice of vaccine for high risk groups

2 to 23 months of age
Based on available published data in this age group, Menveo™ should be used because it has been found to be safe and immunogenic. Routine meningococcal C conjugate vaccine does not need to be administered in addition to Menveo™.

24 months to 55 years of age
Either Men-C-ACYW-135 vaccine may be used.

56 years of age and older
Either Men-C-ACYW-135 vaccine should be considered.

Refer to *Schedule* for additional information, *Table 1* for recommended vaccination for certain travellers and *Table 3* for recommended vaccination of high risk individuals with underlying medical conditions.

PERSONS WITH INADEQUATE IMMUNIZATION RECORDS

Children and adults lacking adequate documentation of immunization should be considered unimmunized and started on an immunization schedule appropriate for their age and risk factors. Conjugate meningococcal vaccine, as appropriate for age, may be given regardless of possible previous receipt of the vaccine as adverse events associated with repeated immunization have not been demonstrated. Refer to *Immunization of Children and Adults with Inadequate Immunization Records* in Part 3 for additional general information.

PREGNANCY AND BREASTFEEDING

Conjugate meningococcal vaccines have not been studied in pregnancy; however, there is no theoretical reason to suspect adverse events will occur and, in circumstances in which the benefits outweigh the risks, the use of conjugate meningococcal vaccines in pregnancy may be considered. Inactivated vaccines, such as conjugate meningococcal vaccines, may be administered to women who are breastfeeding. Refer to *Immunization in Pregnancy and Breastfeeding* in Part 3 for additional general information.

INFANTS BORN PREMATURELY

Premature infants in stable clinical condition should be immunized with conjugate meningococcal vaccine at the same chronological age and according to the same schedule as full-term infants. Infants born prematurely (especially those weighing less than 1,500 grams at birth) are at higher risk of apnea and bradycardia following vaccination. Hospitalized premature infants should have continuous cardiac and respiratory monitoring for 48 hours after their first immunization. Refer to *Immunization of Infants Born Prematurely* in Part 3 for additional general information.

PATIENTS/RESIDENTS IN HEALTH CARE INSTITUTIONS

Residents of long-term care facilities should receive meningococcal vaccine as appropriate for their risk factors. Refer to *Immunization of Patients in Health Care Institutions* in Part 3 for additional general information.

IMMUNOCOMPROMISED PERSONS

Quadrivalent conjugate meningococcal vaccine is recommended for certain high risk individuals as outlined under *High risk groups* above. When considering immunization of an immunocompromised person, consultation with the individual's attending physician may be of assistance in addition to the guidance provided below. For complex cases, referral to a physician with expertise in either or immunization and immunodeficiency is advised.

Congenital (primary) immunodeficiency

Persons with complement, properdin, factor D or primary antibody deficiencies should be vaccinated with Men-C-ACYW-135 vaccine. Refer to *Table 3* for additional information.

Acquired (secondary) immunodeficiency

Hematopoietic stem cell transplantation (HSCT- autologous or allogeneic)

For children and adults, the effect of any previous meningococcal vaccine will be diminished following HSCT; therefore, HSCT recipients should be vaccinated as per recommendations for the previously unvaccinated based on their age or risk factors for IMD. If routinely indicated based on age or other risk factors, conjugate meningococcal vaccine can be given as early as 6 months after transplantation, unless needed earlier for management of a close contact or outbreak. However, if it is given earlier than 6 months after transplant the response may not be optimal and consideration should be given to repeating the dose at least 6 months after transplant (and at least 8 weeks after the previous dose) if ongoing protection is needed.

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Solid organ transplantation

Conjugate meningococcal vaccine (type of vaccine as appropriate for age) is recommended to be given at least two weeks before transplantation if routinely indicated based on age or risk factors for IMD. If not given prior to transplant and routinely indicated based on age or other risk factors, meningococcal vaccine can be given any time after 6 months post-transplant and at least one month after discontinuation of treatment for acute rejection unless needed earlier for management of a close contact or outbreak. However, if it is given earlier than 6 months after transplant or earlier than 1 month after discontinuing treatment for acute rejection, the response may not be optimal and consideration should be given to repeating the dose at least 6 months after transplant and at least 1 month after discontinuing treatment for acute rejection (and at least 8 weeks after the previous dose) if ongoing protection is needed.

HIV-infected

Two doses of Men-C-ACYW-135 vaccine should be considered for individuals with HIV infection. Refer to *Table 3* for additional information.

Acquired complement deficiency

People with conditions such as paroxysmal nocturnal hemoglobinuria who are receiving the terminal complement inhibitor eculizumab (Soliris™) should receive two doses of Men-C-ACYW-135 vaccine. They must be vaccinated at least two weeks prior to receiving the first dose of eculizumab, if possible, and every 5 years thereafter if they continue to use the drug. Refer to *Table 3* for additional information.

Refer to *Booster doses and re-immunization* for additional information and *Immunization of Immunocompromised Persons* in Part 3 for additional general information.

PERSONS WITH CHRONIC DISEASES

Asplenia

Two doses of Men-C-ACYW-135 vaccine are recommended for persons with anatomic or functional asplenia (including sickle cell disease). When elective splenectomy is planned, all recommended vaccines should ideally be completed at least 2 weeks before surgery; if only one dose can be given before surgery, the second dose should be given 8 weeks after the first dose (with a minimum interval of 4 weeks). In the case of an emergency splenectomy, two doses of vaccine should ideally be given beginning 2 weeks after surgery but can be given earlier, before discharge, if the person might not return for vaccination after discharge. Note that persons one year of age and older with asplenia who have not received Men-C-ACYW-135 vaccine should receive two doses administered 8 weeks apart (with a minimum interval of 4 weeks). Periodic booster doses are also recommended.

Refer to *Table 3* for vaccination recommendations of high risk individuals due to underlying conditions based on age. Refer to *Booster doses and re-immunization* for additional information and *Immunization of Persons with Chronic Diseases* in Part 3 for additional general information.

TRAVELLERS

Travellers going to destinations where risk of meningococcal transmission is high should be vaccinated with Men-C-ACYW-135 vaccine. Men-C-C vaccine alone is not appropriate for protection of travellers as it does not protect against serogroup A, which is endemic in selected regions of the world, or serogroup W-135 disease. Current meningococcal disease outbreak information is available from the WHO at: Global Alert and Response (GAR) – Meningococcal Disease. (http://www.who.int/csr/don/archive/disease/meningococcal_disease/en/)

For travellers 2 months to 10 years of age, Men-C-ACYW-135 vaccine is indicated. For children 2 to 23 months, Menveo™ is recommended based on expert opinion and clinical trial data; however, Menveo™ is not authorized for use in this age group. For children 2 years to 10 years of age, Men-C-C vaccine should

already have been administered. If Men-C-C vaccine has not been given previously, it should be administered to children at least 4 weeks after the Men-C-ACYW-135 vaccine. Refer to *Table 1* for recommended immunization for travellers to destinations where risk of meningococcal transmission is high.

Refer to the Committee to Advise on Tropical Medicine and Travel (CATMAT) information on assessing a traveller's need for pre-travel vaccination. (http://www.phac-aspc.gc.ca/tmp-pmv/catmat-ccmtmv/)

Proof of meningococcal immunization may be required by certain countries. For example, Saudi Arabia requires proof of meningococcal immunization for pilgrims to the Hajj in Mecca. (http://www.hajinformation.com/main/p3001.htm) For travel to the Hajj, re-immunization at an interval of less than 5 years from the last dose may be required. Refer to *Immunization of Travellers* in Part 3 for additional general information.

Table 1: Recommended immunization for travellers to destinations where risk of meningococcal transmission is high, not previously immunized with Men-C-ACYW-135[*1] vaccine.

Age	Recommended vaccine(s)	Schedule
2 to 11 months of age	Menveo™[*2]	2 or 3 doses given 8 weeks apart (with another dose between 12-23 months of age that is at least 8 weeks from the previous dose)[*3] and booster doses[*4]
12 to 23 months of age	Menveo™[*2]	2 doses at least 8 weeks apart[*3] and booster doses[*4]
24 months of age and older[*6]	Men-C-ACYW-135[*1]	1 dose[*5] and booster doses[*4]

[*1] Men-C-ACYW-135: Menactra® or Menveo™

[*2] Menveo™ is not authorized for use in children less than 2 years of age; there are no authorized schedules for these children. The schedules in this table are based on those used in published clinical trials and the recommendation that a dose of meningococcal conjugate vaccine be given in the second year of life (12 to 23 months) for children vaccinated at less than 1 year of age.

[*3] Doses may be given a minimum of 4 weeks apart if accelerated immunization needed

[*4] A booster dose should be given every 3 to 5 years if vaccinated at 6 years of age or younger and every 5 years for those vaccinated at 7 years of age and older. Travellers to the Hajj should check recommendations for re-vaccination as more frequent re-vaccination may be required. (http://www.hajinformation.com/main/p3001.htm)

[*5] Children 2 to 10 years of age should have already received Men-C-C vaccine. If not, it should be administered 4 weeks after the Men-C-ACYW-135 vaccine.

[*6] Men-C-ACYW-135 vaccines are not authorized for use in those 56 years of age and older; however, based on limited evidence and expert opinion its use is considered appropriate.

PERSONS NEW TO CANADA

Health care providers who see persons newly arrived in Canada should review the immunization status and update immunization for these individuals. Review of meningococcal vaccination status is particularly important for persons from areas of the world where sickle cell disease is present as persons with sickle cell disease are at risk of serious meningococcal infections. In many countries outside of Canada, conjugate meningococcal vaccines are in limited use. Information on vaccination schedules in other countries can be found on the following website: http://www.who.int/vaccines/GlobalSummary/Immunization/ScheduleSelect.cfm. Refer to *Immunization of Persons New to Canada*) in Part 3 for additional general information.

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WORKERS

Laboratory workers

Research, industrial and clinical laboratory personnel who are potentially routinely exposed to *N. meningitidis* should be offered one dose of Men-C-ACYW-135 vaccine. Re-vaccination is generally recommended every 5 years. Routine infection control precautions should be practiced at all times to minimize the risk of exposure in laboratory workers and post-exposure prophylaxis should be offered after recognized exposures. Refer to *Booster doses and re-immunization* for additional information.

Health care workers (HCW)

There is no evidence to recommend routine meningococcal immunization of HCW. Nosocomial transmission of IMD is very uncommon. HCW are considered as close contacts only if they have had intensive, unprotected contact (without wearing a mask) with infected patients (e.g., intubating, resuscitating or closely examining the oropharynx). It is recommended that HCW use barrier precautions to avoid direct contact with respiratory secretions of patients with meningococcal disease until the patient has completed 24 hours of effective antibiotic therapy.

Military personnel

Military personnel may be at increased risk when accommodated in close quarters or through deployment to endemic or epidemic countries.

Refer to *Immunization of Workers* in Part 3 for additional general information.

POST-EXPOSURE MANAGEMENT

Contacts of cases

Close contacts of individuals with meningococcal infections have an increased risk of developing IMD; this risk is greatest for household contacts. The increased risk of disease for household contacts persists for up to 1 year after disease in the index case and beyond any protection from antibiotic chemoprophylaxis. In general, this prolonged risk is not seen in contacts who do not have ongoing exposure.

Chemoprophylaxis should be offered to all persons having close contact with a case of IMD from 7 days before onset of symptoms in the case to 24 hours after onset of effective treatment in the case, regardless of their immunization status. Refer to the Public Health Agency of Canada *Guidelines for the Prevention and Control of Meningococcal Disease* for information about chemoprophylaxis in the management of close contacts of individuals with meningococcal infection. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/05vol31/31s1/index-eng.php)

Vaccination or re-vaccination of certain close contacts should be considered in addition to chemoprophylaxis when the serogroup is vaccine preventable as it may further reduce the risk of subsequent meningococcal disease.

Close contacts requiring chemoprophylaxis and consideration for immunoprophylaxis

The following individuals (regardless of immunization status) should receive chemoprophylaxis and, if the meningococcal serogroup identified in the case of IMD is vaccine preventable, should also be considered for immunoprophylaxis:

- Household contacts of a case of IMD
- Persons who share sleeping arrangements with a case of IMD
- Persons who have direct nose or mouth contamination with oral or nasal secretions of a case of IMD (e.g., kissing on the mouth, shared cigarettes, shared drinking bottles)
- Children and staff in contact with a case of IMD in child care or nursery school facilities

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Refer to *Table 2* for specific recommendations for immunoprophylaxis of close contacts of IMD cases according to the serogroup in the index case and the age and underlying conditions of the contact.

Re-vaccination criteria for those previously vaccinated against IMD

The following provides criteria for the re-vaccination of previously vaccinated close contacts when the index case has a vaccine preventable IMD serogroup or there is a vaccine preventable outbreak of IMD:

- Those previously vaccinated with a serogroup that differs from the index case or outbreak strain should be vaccinated immediately with the appropriate vaccine (as outlined in *Table 2*);
- Those previously vaccinated with a serogroup that is the same as the index case or outbreak strain should be re-vaccinated with the appropriate vaccine (as outlined in *Table 2*):
  - If they were less than 1 year of age at last meningococcal vaccination and more than **4 weeks** has passed since their last meningococcal vaccine;
  - If they have an underlying medical condition that puts them at risk for meningococcal disease and more than **4 weeks** has passed since their last meningococcal vaccine;
  - If more than **a year** has passed since their last meningococcal vaccine if they were not less than 1 year of age at the time of their last meningococcal vaccination and if they have no underlying medical condition that puts them at risk for meningococcal disease.

Close contacts requiring chemoprophylaxis only

The following individuals should receive chemoprophylaxis only, immunoprophylaxis is not necessary:

- Health care workers who have had **intensive unprotected contact** (without wearing a mask) with infected patients (i.e., intubating, resuscitating or closely examining the oropharynx).
- Airline passengers sitting immediately on either side of the case (but not across the aisle) when the total time spent aboard the aircraft was at least 8 hours.
- Close contacts of a case of IMD due to serogroups not present in meningococcal vaccines, or when the serogroup in the index case has not been determined.
- Previously vaccinated close contacts who do not meet the criteria for re-vaccination as outline above

OUTBREAK CONTROL

Outbreaks of meningococcal disease

Consultation with either or public health officials and experts in communicable disease is important in the assessment and control of meningococcal disease outbreaks. Outbreaks may be controlled by the use of a conjugate meningococcal vaccine. The type of vaccine to use in an outbreak is dependent on the serogroup causing the outbreak and the age of those being vaccinated as outlined in *Table 2*. Re-vaccination criteria of previously vaccinated individuals are outlined above in *Re-vaccination criteria for those previously vaccinated against IMD*.

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Table 2: Recommended vaccination of close contacts for post-exposure management and for outbreak control

Group	Recommended vaccine(s)	Schedule
Close contacts and outbreak control of **serogroup C** invasive meningococcal disease		
2 months to less than 12 months of age	Men-C-C*[1]	***Unvaccinated:*** 1 dose immediately after exposure then complete the routine series of Men-C-C ***Previously vaccinated:*** If previously vaccinated then re-vaccinate with Men-C-C if at least **4 weeks** since last dose, then complete the routine series of Men-C-C if necessary
12 months – 10 years of age	Men-C-C*[1]	***Unvaccinated:*** 1 dose immediately after exposure ***Previously vaccinated:*** If previously vaccinated at less than 1 year of age OR person is at high risk for IMD due to underlying medical conditions*[2], then re-vaccinate with one dose of Men-C-C if at **least 4 weeks** since last dose; otherwise re-vaccinate if at least **1 year** since last dose
11 years of age and older	Men-C-C*[1] OR Men-C-ACYW-135*[3]	***Unvaccinated:*** 1 dose immediately after exposure ***Previously vaccinated:*** If previously vaccinated at less than 1 year of age OR person is at high risk for IMD due to underlying medical conditions*[2], then re-vaccinate with one dose of vaccine of choice if at least **4 weeks** since last dose; otherwise re-vaccinate if at least **1 year** since last dose
Close contacts and outbreak control of **serogroup A, Y, or W-135** invasive meningococcal disease		
2 months to less than 12 months of age	Menveo™*[4]	***Unvaccinated:*** 2 or 3 doses given 8 weeks apart with another dose between 12 and 23 months and at least 8 weeks from the previous dose ***Previously vaccinated:*** • If previously vaccinated with only Men C-C, give Menveo™ as for unvaccinated persons, regardless of when Men-C-C was previously given*[5] • If previously vaccinated with Men-C-ACYW-135, then re-vaccinate with one dose of Menveo™ if at least **4 weeks** since last dose of Men-C-ACYW-135 vaccine; then complete series

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Group	Recommended vaccine(s)	Schedule
12 to 23 months of age	Menveo™*4	***Unvaccinated:*** 2 doses at least 8 weeks apart ***Previously vaccinated:*** • If previously vaccinated with only Men C-C, give Menveo™ as for unvaccinated persons, regardless of when Men-C-C was previously given*5 • If previously vaccinated with Men-C-ACYW-135 at less than 1 year of age OR if person is at high risk for IMD due to underlying medical conditions*2, then re-vaccinate with one dose of Menveo™ if at least **4 weeks** since last dose of Men-C-ACYW-135; otherwise re-vaccinate with one dose of Menveo™ if at least **1 year** since last dose of Men-C-ACYW-135
2 years and older	Men-C-ACYW-135*3	***Unvaccinated:*** 1 dose immediately after exposure*6 ***Previously vaccinated:*** • If previously vaccinated with only Men C-C, give Men-C-ACYW-135 as for unvaccinated persons, regardless of when Men-C-C was previously given*5 • If previously vaccinated with Men-C-ACYW-135 at less than 1 year of age OR if person is at high risk for IMD due to underlying medical conditions*2, then re-vaccinate with one dose of Men-C-ACYW-135 if at least **4 weeks** since last dose of Men-C-ACYW-135; otherwise re-vaccinate with one dose of Men-C-ACYW-135 if at least **1 year** since last dose of Men-C-ACYW-135

*1 Men-C-C: Meningitec® or Menjugate® or NeisVac-C®

*2 At high risk due to underlying medical conditions -refer to *Underlying medical conditions*

*3 Men-C-ACYW-135: Menactra® or Menveo™

*4 Menveo™ is not authorized for use in children less than 2 years of age; there are no authorized schedules for these children. The schedules in this table are based on those used in published clinical trials and the recommendation that a dose of meningococcal conjugate vaccine be given in the second year of life (12 to 23 months) for children vaccinated at less than 1 year of age.

*5 In general, a minimum four week interval is recommended between doses of conjugate meningococcal vaccines; however, in an outbreak or to manage a close contact of a case of IMD, the second dose of conjugate meningococcal vaccine may be given as soon as indicated to provide protection to a close contact who is unvaccinated for the implicated serogroup.

*6 Individuals at high risk due to underlying medical conditions routinely need two doses of Men-C-ACYW-135.

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VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

Dose

Each dose of meningococcal vaccine is 0.5 mL.

Route of administration

Conjugate meningococcal vaccine should be administered intramuscularly (IM). Refer to *Vaccine Administration Practices* in Part 1 for additional information.

Schedule

Recommended meningococcal immunization schedules and products vary across provinces/territories depending upon the epidemiology of meningococcal disease in the jurisdiction and other programmatic factors.

Healthy infants and children (2 to 23 months of age)

The manufacturer-recommended infant schedule varies with the Men-C-C vaccine used. For routine infant immunization, three doses of Menjugate® may be administered separated by at least 4 weeks, from 2 months of age. Two doses of NeisVac-C® or Meningitec® may be administered at least 2 months apart, from 2 months of age. **If Men-C-C vaccine is given to infants less than 12 months of age, a booster dose should be given between 12 to 23 months of age.** If the booster dose is missed, it can be given at the next vaccination opportunity.

Healthy children, adolescents and young adults

One dose of Men-C-C vaccine is recommended for previously unimmunized children 12 months to less than 5 years of age and may be considered for children 5 to 11 years of age. In addition to routine Men-C-C vaccine for infants and young children, adolescents and young adults (12 to 24 years of age) should receive one dose of either Men-C-C or Men-C-ACYW-135 vaccine, based on local epidemiology and programmatic considerations, with around 12 years being the preferred age for the routine dose

High risk individuals due to underlying medical conditions

High risk individuals are those with underlying conditions that make them more likely to develop IMD. Schedule options for high risk individuals who have not previously received a quadrivalent conjugate meningococcal vaccine are included in *Table 3*. As noted in *Table 3*, previously unimmunized high risk persons 12 months of age and older should receive a two dose primary series administered 8 weeks apart (with a minimum interval of 4 weeks).

Table 3: Recommended immunization for high risk groups because of underlying medical conditions[*1] not previously immunized with Men-C-ACYW-135[*2] vaccine

Age	Recommended vaccine(s)	Schedule
2 to 11 months of age	Menveo™[*3]	2 or 3 doses given 8 weeks apart (with another dose between 12-23 months of age that is at least 8 weeks from the previous dose)[*4] and booster doses[*5]
12 to 23 months of age	Menveo™[*3]	2 doses at least 8 weeks apart[*4] and booster doses[*5]
24 months to 55 years of age	Men-C-ACYW-135	2 doses 8 weeks apart[*4] and booster doses[*5]
56 years of age and older	Men-C-ACYW-135[*6]	2 doses 8 weeks apart[*4] and booster doses[*5]

[*1] At high risk due to underlying medical conditions: refer to *Underlying medical conditions*
[*2] Men-C-ACYW-135: Menactra® or Menveo™
[*3] Menveo™ is not authorized for use in children less than 2 years of age; there are no authorized schedules for these children. The schedules in this table are based on those used in published clinical trials and the recommendation that a dose of meningococcal conjugate vaccine be given in the second year of life (12 to 23 months) for children vaccinated at less than 1 year of age.
[*4] Doses may be given a minimum of 4 weeks apart if accelerated immunization needed
[*5] A booster dose should be given every 3 to 5 years if vaccinated at 6 years of age or younger and every 5 years for those vaccinated at 7 years of age and older.
[*6] Men-C-ACYW-135 vaccines are not authorized for use in those 56 years of age and older; however, based on limited evidence and expert opinion its use is considered appropriate.

BOOSTER DOSES AND RE-IMMUNIZATION

Circulating antibodies are considered necessary to protect an individual against IMD. Re-vaccination is recommended as follows:

- Individuals at high risk of developing meningococcal disease due to underlying conditions as outlined in *Underlying medical conditions*. Re-vaccination is recommended every 3 to 5 years for those vaccinated at 6 years of age and younger and every 5 years for those vaccinated at 7 years of age and older.
- When travelling to areas where meningococcal vaccine is recommended or required. Re-vaccination is recommended every 3 to 5 years of age if vaccinated at 6 years of age and younger, and every 5 years for those vaccinated at 7 years of age and older. Previously vaccinated travellers are advised to check requirements for re-vaccination with meningococcal vaccines prior to travel to the Hajj as more frequent vaccination may be required (refer to *Ministry of Hajj – Kingdom of Saudi Arabia* and *Travellers*). (http://www.hajinformation.com/main/p3001.htm)
- Military personnel who remain at risk due to travel or overcrowded conditions. A booster dose is recommended every 5 years if at ongoing risk
- At the time of exposure for contacts of a case of IMD in some circumstances. Refer to *Post-exposure management*.
- During a community outbreak of IMD in some circumstances. Refer to *Post-exposure management*.
- All laboratory personnel who are potentially routinely exposed to *N. meningitidis*. Booster doses should be given at routine 5 year intervals for those laboratory workers who remain at ongoing risk of exposure. Refer to *Workers*.

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People previously vaccinated with a polysaccharide meningococcal vaccine should be re-vaccinated with the appropriate conjugate meningococcal vaccine if they remain at ongoing risk for meningococcal disease, with at least a 6 month interval following vaccination with polysaccharide meningococcal vaccine.

SEROLOGIC TESTING

Serologic testing is not recommended before or after receiving meningococcal vaccine.

STORAGE REQUIREMENTS

Menactra®, Meningitec®, NeisVac-C®: Store in a refrigerator at +2°C to +8°C. Do not freeze.

Menjugate®, Menveo™: Store in a refrigerator at +2°C to +8°C. Do not freeze. Protect from light.

Refer to *Storage and Handling of Immunizing Agents* in Part 1 for additional general information.

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

Men-C-C vaccine may be administered concomitantly with routine childhood vaccines and Men-C-ACYW-135 vaccine may be administered concomitantly with adolescent and adult age appropriate vaccines at different injection sites using separate needles and syringes.

Menveo™ can be administered with routine paediatric vaccines; however, further studies are needed with regard to concomitant administration with pneumococcal 13-valent conjugate vaccine. Co-administration of Menveo™ and combined tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) may result in a lower immune response to the pertussis antigens than when Tdap vaccine is given alone; however, the clinical significance of this is unknown. Tdap vaccine given one month after Menveo™ induces the strongest immunologic response to pertussis antigens. Refer to *Timing of Vaccine Administration* in Part 1 for additional general information.

VACCINE SAFETY AND ADVERSE EVENTS

Refer to *Vaccine Safety* Part 2 for additional general information.

COMMON AND LOCAL ADVERSE EVENTS

Conjugate meningococcal vaccines

Men-C-ACYW-135 vaccines

Injection site reactions occur in up to 59% of vaccinees. Fever is reported in up to 5% of recipients and systemic reactions, such as headache and malaise, are reported in up to 60% of recipients.

Men-C-C vaccines

Mild reactions, including injection site reactions (redness, tenderness, and swelling), occur in up to 50% of vaccinees. Irritability occurs in up to 80% of infants and fever in up to 9% when other vaccines were administered. Headaches and malaise occur in up to 10% of older children and adults. These reactions last no more than a few days.

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LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

Serious adverse events are rare following immunization and, in most cases, data are insufficient to determine a causal association. A concern regarding Guillain Barre Syndrome (GBS) following Menactra® was raised because of case reports to the United States Vaccine Adverse Event Reporting System (VAERS). Subsequently, two large epidemiologic studies were conducted. No cases of GBS were observed during the six weeks following over 2.2 million doses given to individuals aged 11 to 21 years. This evidence supports the conclusion that there is no increased risk of GBS following Menactra®.

GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Vaccine providers are asked to report, through local public health officials, any serious or unexpected adverse event felt to be temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI. Refer to Reporting Adverse Events Following Immunization (AEFI) (http://www.phac-aspc.gc.ca/im/aefi_guide/index-eng.php) in Canada and Vaccine Safety in Part 2 for additional information about AEFI reporting.

CONTRAINDICATIONS AND PRECAUTIONS

Meningococcal vaccine is contraindicated in persons with a history of anaphylaxis after previous administration of the vaccine and in persons with proven immediate or anaphylactic hypersensitivity to any component of the vaccine or its container. Refer to *Table 1* in *Contents of Immunizing Agent Available for Use in Canada* in Part 1 for lists of all vaccines available for use in Canada and their contents. For meningococcal vaccines, potential allergens include:

- Menactra®: diphtheria toxoid protein
- Meningitec®: latex in vial stopper, diphtheria CRM_{197} toxoid carrier protein Menjugate®: latex in tip cap of syringe, diphtheria CRM_{197} toxoid carrier protein
- Menomune®: thimerosal, latex
- Menveo™: diphtheria CRM_{197} toxoid carrier protein
- NeisVac-C®: tetanus toxoid protein

There are very few individuals who cannot receive meningococcal vaccines. In situations of suspected hypersensitivity or non-anaphylactic allergy to vaccine components, investigation is indicated which may involve immunization in a controlled setting. Consultation with an allergist is advised. Menomune® may be considered in the rare circumstance that someone is allergic to components (other than latex) in the conjugate meningococcal vaccines.

Administration of meningococcal vaccine should be postponed in persons with moderate or severe acute illness. Persons with minor acute illness (with or without fever) may be vaccinated.

Refer to *General Contraindications and Precautions* in Part 2 for additional general information.

OTHER CONSIDERATIONS

INTERCHANGEABILITY OF VACCINES

There are no published data regarding the interchangeability of Men-C-C vaccines, but the vaccines have been safely interchanged without a noticeable decrease in efficacy. When possible, the infant series should be completed with the same vaccine. Either Men-C-ACYW-135 vaccine may be used for re-vaccination, regardless of which meningococcal vaccine was used for initial vaccination. Refer to *Principles of Vaccine Interchangeability* in Part 1 for additional general information.

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PART 4

MUMPS VACCINE

KEY INFORMATION (refer to text for details)

What	• Outbreaks of mumps continue to occur in Canada and the proportion of cases aged 20 years and older has increased. • Complications such as orchitis/oophoritis are relatively frequent; permanent sequelae like deafness are rare. • Mumps vaccine is available as measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) vaccine. • Mumps vaccine effectiveness has been estimated at 62% to 91% for one dose and 76% to 95% for two doses. • Reactions to MMR and MMRV vaccine are generally mild and transient and include pain and redness at the injection site, low-grade fever and rash.
Who	• Mumps-containing vaccine is recommended for routine immunization of children and for immunization of children and adolescents who missed mumps immunization on the routine schedule. • Mumps-containing vaccine is recommended for susceptible adults born in 1970 or later. • Adults born before 1970 can be presumed to have acquired natural immunity to mumps; however, non-immune health care workers, travellers and military personnel should receive MMR vaccine, regardless of year of birth.

How	• **Routine childhood immunization:** administer two doses of mumps-containing vaccine (MMR or MMRV); the first dose at 12 to 15 months of age and the second dose at 18 months of age or any time thereafter, typically before school entry. • **Children and adolescents who are previously unimmunized:** administer two doses of mumps-containing vaccine. The minimum interval between doses of MMR vaccine is 4 weeks. MMRV vaccine may be used in healthy children aged 12 months to 12 years. The recommended interval between 2 doses of MMRV vaccine is at least 3 months; a minimum interval of 6 weeks between doses may be used if rapid, complete protection is required. • **Susceptible adults born in 1970 or later:** administer one dose of MMR vaccine. Those who are at the greatest risk of mumps exposure (travellers to destinations outside of North America, health care workers, students in post-secondary educational settings, and military personnel) should receive two doses of MMR vaccine. • **Non-immune health care workers and military personnel born before 1970:** administer two doses of MMR vaccine at least 4 weeks apart. • **Non-immune travellers born before 1970:** administer one dose of MMR vaccine. • **Non-immune students born before 1970:** consider administering one dose of MMR vaccine
Why	• Mumps occurs worldwide and outbreaks continue to occur. • Complications of mumps disease are relatively frequent although permanent sequalae are rare. • MMR and MMRV vaccines are safe and effective.

Since the publication of the *2006 Canadian Immunization Guide:*

- New recommendations have been made regarding a two dose mumps-containing vaccine vaccination schedule for children.
- New recommendations have been made regarding mumps vaccination in adults.
- A new combined multivalent vaccine (measles-mumps-rubella-varicella vaccine [MMRV]) has become available for children aged 12 months to 12 years.

For additional information, refer to the National Advisory Committee on Immunization (NACI) Statements: *Statement on Measles-Mumps-Rubella-Varicella Vaccine* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-9/index-eng.php); *Updated Recommendations for the use of Varicella and MMR Vaccines in HIV-infected Individuals* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-7/index-eng.php); and Statement on mumps vaccine, (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/acs-08/index-eng.php)

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Mumps virus is a member of the *Paramyxoviridae* family.

Reservoir

Humans

Transmission

Mumps virus is transmitted primarily by droplet spread as well as direct contact with saliva of an infected person. The incubation period is about 16 to 18 days. Virus has been isolated from saliva 7

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days before to 9 days after the onset of parotitis with maximum infectiousness between 2 days before to 5 days after onset of symptoms.

Risk factors

In general, people who have not had mumps or who have not been successfully vaccinated are at risk of being infected. In Canada, adults born before 1970 can be presumed to have acquired natural immunity to mumps; however, some individuals may be susceptible. A second dose of mumps vaccination was routinely given along with measles and rubella (MMR) for measles control beginning in 1996 to 1997. Depending on the age the second dose was given, people born before 1996 may only have received one done of mumps-containing vaccine and so may still be susceptible. In addition, people born between 1970 and approximately 1996 who received only one dose of mumps-containing vaccine may still be susceptible. Adolescents and adults who are at greatest risk of exposure to mumps include students in secondary and post-secondary educational settings, military personnel, health care workers and travellers to destinations outside of North America.

Seasonal/temporal pattern

Historically, the incidence of mumps peaked in the spring and winter months in temperate zones, but now there are sporadic cases and outbreaks.

Spectrum of clinical illness

About 40% of those infected with mumps develop acute parotitis, which is unilateral in about 25% of cases. Non-specific or primarily respiratory symptoms occur in about one-half of those infected. Subclinical infection is common. Although complications are relatively frequent, permanent sequelae are rare. Before the widespread use of vaccine, mumps was a major cause of viral meningitis. Mumps meningoencephalitis can, rarely, result in permanent neurologic sequelae, including paralysis, seizures, cranial nerve palsies and hydrocephalus. Permanent deafness may occur, at an estimated rate of 0.5 to 5.0 per 100,000 mumps cases. Orchitis occurs in 20% to 30% of post-pubertal male cases and oophoritis in 5% of post-pubertal female cases. Involvement of the reproductive organs is commonly unilateral; therefore, sterility is rare. Mumps infection in pregnancy has not been associated with congenital malformations, but mumps infection during the first trimester of pregnancy may increase spontaneous abortion.

DISEASE DISTRIBUTION

Incidence/prevalence

Global

Mumps occurs worldwide with cases reported throughout the year and epidemics occurring every two to five years. Mumps remains endemic in many countries, and mumps vaccine is used in only 59% of World Health Organization (WHO) member states.

Between 2004 and 2006, there was a large mumps outbreak in the United Kingdom (UK), with more than 70,000 cases. In 2006 there was a multi-state outbreak in the United States (US) with over 2,500 cases. In 2009 there were more than 7,400 cases of mumps in England and Wales, mostly among unvaccinated young adults. In June 2009, a large outbreak of mumps occurred in New York and New Jersey in the US. The outbreak mainly affected school age males from a faith-based community. Of those with known vaccination status, 88% had received at least one dose of mumps-containing vaccine before the outbreak and 75% had received two doses.

National

Since the approval of mumps vaccine in 1969, the number of reported mumps cases has decreased by more than 99% from an average of 34,000 cases reported per year in the early 1950s to fewer than 400 cases per year in the early 1990s. A further reduction in incidence was observed following the introduction of the routine second dose of MMR vaccine in 1996 to 1997. The annual number of cases has continued to decrease; during the period 2000 to 2006, an average of 81 cases were reported

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annually, ranging from 28 (2003) to 201 cases (2002). However, in 2007 there were over 1,000 cases and in 2008 there were almost 750 reported cases, mainly as a result of outbreaks in several provinces.

The age distribution of mumps in Canada has changed. While the total number of reported cases decreased, the proportion of reported cases aged 20 years and older increased from 14% in 1988-1990 to 64% in 2003-2005. Conversely, the proportion of cases aged 1 to 9 years fell from 49% to 17% during the same period.

RECENT OUTBREAKS

In Canada, large outbreaks of mumps have been rare in recent years. In 2007, large outbreaks occurred in Nova Scotia, New Brunswick and Alberta with a total of 1,159 confirmed cases, accounting for 90% of the total cases in Canada that year. The majority (58%) of cases occurred in persons aged 20 to 29 years, many of who were college or university students. Immunization history was known for less than one-half of the mumps cases. Of those known, 8% had received two or more doses, 73% had received one dose, and 19% had received no mumps immunization. The viral strain in the 2007 outbreaks was identical to the strain (genotype G) detected in the previous Nova Scotia outbreaks, the 2006 US multi-state outbreak, and the UK epidemic.

In 2008, large outbreaks occurred in Alberta, Ontario and British Columbia (BC). In Alberta, the 2007 outbreak continued with an additional 280 cases in 2008. In Ontario, a total of 324 outbreak cases were reported, of which 289 were confirmed. The cases ranged in age from less than 1 year to 45 years (average age 11) with no gender difference. The majority of cases (95.7%) occurred in unimmunized individuals. The BC outbreak included 183 reported cases, of which 133 were confirmed. The outbreak started in a largely unimmunized faith-based community. One-half of the cases were in the 0 to 19 year old age group. Nearly one-half of the cases (46%) were unimmunized and 28% of the cases had unknown immunization history.

Beginning in October 2009, an outbreak of mumps occurred among a faith-based community in Quebec with 23 confirmed cases. The outbreak was linked to a large mumps outbreak in New York and New Jersey in the US. All cases were male and aged 8 to 47 years.

PREPARATIONS AVAILABLE FOR USE IN CANADA

MUMPS-CONTAINING VACCINES

- **M-M-R® II** (live, attenuated combined measles, mumps and rubella vaccine), Merck Canada Inc. (MMR)
- **PRIORIX®** (live, attenuated combined measles, mumps and rubella vaccine), GlaxoSmithKline Inc. (MMR)
- **PRIORIX-TETRA®** (live, attenuated combined measles, mumps, rubella and varicella vaccine), GlaxoSmithKline Inc. (MMRV)

In Canada, mumps vaccine is only available in combination with measles and rubella vaccine (MMR) or measles, rubella and varicella vaccine (MMRV). In many countries outside of Canada, measles vaccine alone is given and mumps vaccination is not offered.

For complete prescribing information, consult the product leaflet or information contained within the product monograph available through the Health Canada's Drug Product Database, (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php) Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 for a list of vaccines available for use in Canada and their contents.

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EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

EFFICACY AND EFFECTIVENESS

Mumps vaccine effectiveness has been estimated at 62% to 91% for one dose and 76% to 95% for two doses. Mumps outbreaks have been reported in populations with greater than 95% coverage with single dose mumps-containing vaccine, suggesting that one dose of mumps-containing vaccine is not sufficient to prevent mumps outbreaks. In some instances, outbreaks have arisen in settings with high two-dose coverage. Waning immunity contributes to the risk of mumps in vaccinated individuals. There are no data regarding the efficacy of MMRV vaccine.

IMMUNOGENICITY

In clinical studies a single injection of MMR vaccine induced measles antibodies in 95%, mumps antibodies in 96%, and rubella antibodies in 99% of previously seronegative children.

In a study of 12 month old children, a single dose of MMRV vaccine resulted in a seroconversion rate for measles, mumps, rubella and varicella of 98%, 97%, 98% and 93%, respectively. The seroconversion rates and geometric mean titres for individual components were not significantly different from those achieved after MMR vaccine alone. A study of children receiving two doses of MMRV vaccine during the second year of life noted seropositivity for measles, mumps, rubella and varicella of 99%, 97.4%, 100% and 99.4% respectively by the third year post-vaccination. Long-term persistence of anti-measles, anti-mumps, anti-rubella and anti-varicella antibodies following MMRV vaccinations are under evaluation.

RECOMMENDATIONS FOR USE

CHILDREN (12 months to 17 years of age)

Two doses of mumps-containing vaccine should be given for routine immunization of children and for immunization of children and adolescents who missed mumps immunization on the routine schedule. MMRV vaccine may be used in children aged 12 months to 12 years.

Students in secondary educational settings should have documented evidence of receiving two doses of mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease.

ADULTS (18 years of age and older)

Routine immunization: adults **born before 1970** are generally presumed to have acquired natural immunity to mumps; however, some of these individuals may be susceptible. Adults without contraindications, **born in 1970 or later** who do not have documented evidence of receiving mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps infection should be immunized with one dose of MMR vaccine.

Health care workers, regardless of their year of birth, who do not have documented evidence of receiving two doses of mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should receive two doses of MMR vaccine. Refer to *Workers*.

Students in post-secondary educational settings, **born in 1970 or later**, who do not have documented evidence of receiving two doses of mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should receive two doses of MMR vaccine. In students **born before 1970**, administration of one dose of MMR vaccine should be considered.

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Military personnel, regardless of their year of birth, who do not have documented evidence of receiving two doses of a mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should receive two doses of MMR vaccine.

Travellers to destinations outside of North America, **born in 1970 or later**, who do not have documented evidence of receiving two doses of mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should receive two doses of mumps-containing vaccine. Travellers **born before 1970** who do not have documented evidence of receiving a mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should receive one dose of MMR vaccine. Refer to *Travellers*.

Table 1 provides a summary of criteria for mumps immunity. Refer to *Schedule*.

Table 1: Criteria for immunity to mumps

Routine	Health care workers	Travellers to destinations outside North America	Students in secondary or post-secondary educational settings	Military personnel
Documentation of vaccination: • Children 12 months to 17 years of age: 2 doses[1] • Adults born in 1970 or later: 1 dose[1, 2] **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity **OR** Born before 1970	Documentation of vaccination with 2 doses[1] (regardless of year of birth) **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity	Documentation of vaccination: • If born in 1970 or later: 2 doses[1] • If born before 1970: 1 dose[1] **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity	Documentation of vaccination: • If born in 1970 or later: 2 doses[1] • If born before 1970: consider 1 dose[1] if no documentation of receipt of mumps-containing vaccine **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity	Documentation of vaccination with 2 doses[1] (regardless of year of birth) **OR** History of laboratory confirmed infection **OR** Laboratory evidence of immunity

1 Mumps-containing vaccine
2 Refer to additional recommendations for health care workers, travellers to destinations outside of North America, students in post-secondary educational settings and military personnel

PERSONS WITH INADEQUATE IMMUNIZATION RECORDS

Children and adults lacking adequate documentation of immunization should be considered unimmunized and started on an immunization schedule appropriate for their age and risk factors, unless known to be immune based on laboratory testing. MMR or MMRV vaccine, as appropriate, may be given regardless of possible previous receipt of the vaccine because additional adverse events associated with repeated

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immunization have not been demonstrated. Refer to Immunization of Persons with Inadequate Immunization Records in Part 3 for additional general information.

PREGNANCY AND BREASTFEEDING

Immunity to measles, mumps and rubella should be reviewed in women of reproductive age, and vaccination should be recommended to non-pregnant susceptible women. Ideally, the immunization status of women intending to become pregnant should be reviewed and vaccines updated as necessary prior to conception. Women should delay pregnancy by at least 28 days following vaccination with a live vaccine.

MMR and MMRV vaccines should generally not be given during pregnancy because of the theoretical risk of disease transmission to the fetus; however, there is no evidence demonstrating a teratogenic or other risk from such vaccines. There was no evidence of Congenital Rubella Syndrome in any of the offspring of 226 women inadvertently vaccinated during pregnancy. Inadvertent immunization with MMR vaccine is not a reason for pregnancy termination. In some situations, potential benefits of MMR vaccination may outweigh risks such as during measles or rubella outbreaks, in which case vaccination may be considered.

Women who are breastfeeding can be vaccinated with MMR vaccine.

Refer to Contraindications and Precautions. Refer to Immunization in Pregnancy and Breastfeeding in Part 3 for additional general information.

IMMUNOCOMPROMISED PERSONS

In general, immunocompromised persons should not receive live vaccines because of the risk of disease caused by the vaccine strains. When considering immunization of an immunocompromised person with a live vaccine, **approval from the individual's attending physician should be obtained before vaccination.** For complex cases, referral to a physician with expertise in immunization or immunodeficiency or both is advised. Refer to Immunocompromised persons in the Measles Vaccine in Part 4 for additional information.

Household contacts

Susceptible household contacts of immunocompromised people should receive a mumps-containing vaccine as appropriate for age and risk factors.

Refer to Contraindications and Precautions. Refer to Immunization of Immunocompromised Persons in Part 3 for additional information.

PERSONS WITH CHRONIC DISEASES

Neurologic disorders

People with conditions such as autism spectrum disorders or demyelinating disorders (including multiple sclerosis) should receive all routinely recommended immunizations, including MMR or MMRV vaccine. Refer to Immunization of Persons with Chronic Diseases in Part 3 for additional general information.

TRAVELLERS

Protection against mumps is especially important for people planning travel to destinations outside of North America. Travellers born in 1970 or later, who do not have documented evidence of receiving two doses of mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should receive two doses of mumps-containing vaccine.

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Travellers born before 1970, who do not have documented evidence of receiving mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should receive one dose of MMR vaccine.

Mumps is endemic in many countries. Refer to mumps incidence rates in WHO member countries for additional information. (http://www.who.int/immunization_monitoring/diseases/en/)

Refer to Immunization of Travellers in Part 3 for additional general information.

PERSONS NEW TO CANADA

Health care providers who see persons newly arrived in Canada should review the immunization status and update immunization for these individuals. In many countries outside of Canada, mumps and rubella vaccines are in limited use and measles vaccine alone is given. A Canadian study showed that more than one-third of new immigrants and refugees, particularly women, were susceptible to measles, mumps, or rubella. Refer to Immunization of Persons New to Canada in Part 3 for additional general information.

WORKERS

It is recommended that all health care workers be immune to mumps. Health care workers, regardless of their year of birth, who do not have documented evidence of receiving two doses of mumps-containing vaccine on or after their first birthday, or laboratory evidence of immunity, or a history of laboratory confirmed mumps disease should be vaccinated accordingly so that they have received two doses of MMR vaccine. Refer to Immunization of Workers in Part 3 for additional general information.

POST-EXPOSURE IMMUNIZATION

Post-exposure MMR vaccination does not prevent or alter the clinical severity of mumps. It may be considered if repeated exposure to mumps is anticipated. If exposure to mumps does not cause infection, post-exposure vaccination with MMR vaccine should induce protection against subsequent infection. There is no evidence of increased risk of adverse reactions from immunization with MMR vaccine if an individual is already immune to one or more components of the vaccine or infected by mumps virus.There are no data on the use of MMRV vaccine in post-exposure situations. Passive immunization with human immune globulin (Ig) is not effective in preventing mumps.

OUTBREAK CONTROL

With the implementation of a two dose schedule for mumps vaccine, it is expected that large outbreaks of mumps will occur less frequently. However, cases that do occur may result in transmission of mumps, usually among unvaccinated children and young adults who have not received two doses of vaccine and who were born after wide circulation of natural mumps disease was common. Outbreaks have also occurred in populations who are predominantly vaccinated with two doses of mumps-containing vaccines. In outbreak situations, a dose of mumps-containing vaccine is, recommended for those born in or after 1970 who received only one dose of a mumps-containing vaccine. At-risk populations will need to be further defined by the age groups and settings involved in the outbreak. For further information regarding mumps outbreak control refer to the Public Health Agency of Canada's (PHAC) Supplement: Guidelines for the Prevention and Control of Mumps Outbreaks in Canada. (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/36s1/index-eng.php)

VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

Dose

Each dose is 0.5 mL.