

Public Health and Primary Health Care
Communicable Disease Control
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November, 2015

Re: Rubella and Congenital Rubella Syndrome/Infection Reporting and Case Investigation

Reporting of rubella (Rubella virus) and congenital rubella syndrome/infection is as follows:

Laboratory:

- All positive laboratory results for Rubella virus are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044).

Health Care Professional:

- Probable (clinical) cases of **rubella** are reportable to the Public Health Surveillance Unit by telephone (204-788-6736) during regular hours (8:30 a.m. to 4:30 p.m.) AND by secure fax (204-948-3044) on the **same day** that they are identified. After hours telephone reporting is to the Medical Officer of Health on call at (204-788-8666). The *Clinical Notification of Reportable Diseases and Conditions* form (<http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf>) should be used.
- Probable (clinical) cases of **congenital rubella syndrome** are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044) within 5 business days of being identified. The *Clinical Notification of Reportable Diseases and Conditions* form (<http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf>) should be used.
- Cooperation in Public Health investigation is appreciated.

Regional Public Health/First Nations Inuit Health Branch (FNIHB):

- Once the case has been referred to Regional Public Health/FNIHB, the *Communicable Disease Control Investigation Form* (<http://www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf>) should be completed and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

Sincerely,

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1. Case Definition

1.1 Rubella

1.11 *Confirmed Case*

Consistent clinical illness^a with laboratory confirmation of infection in the absence of recent immunization^b with rubella-containing vaccine. Laboratory confirmation includes at least one of:

- Isolation of rubella virus from an appropriate clinical specimen (e.g., nasal or throat swab, urine)
OR
- Detection of rubella virus by nucleic acid amplification test (NAAT) (e.g., throat swab or urine specimen) (NAAT for rubella is currently not available in Manitoba)
OR
- Seroconversion or a significant rise in rubella IgG titre between acute and convalescent sera by any standard serologic assay
OR
- Positive test for rubella IgM antibody using a recommended assay^c in a person with an epidemiologic link to a laboratory-confirmed case or who has recently travelled to an area of known rubella activity.
OR

Clinical illness^a in a person with an epidemiologic link to a laboratory-confirmed case (1).

1.12 *Probable Case*

Clinical illness^a in the absence of appropriate laboratory tests and in the absence of an epidemiological link to a laboratory confirmed case in a person who has recently been to an area of known rubella activity (1).

Note: Surveillance for rubella focuses on evident disease rather than infection. Therefore, surveillance definitions do not take into account asymptomatic or subclinical infections that may be detectable by laboratory methods.

1.2 Congenital Rubella Syndrome (CRS)

1.21 *Confirmed Case*

Live Birth: two clinically compatible manifestations (any combination from A and/or B below) with laboratory confirmation of infection: Laboratory confirmation includes at least one of:

- Isolation of rubella virus from an appropriate clinical specimen (e.g., nasal or throat swab, blood, urine, cerebrospinal fluid)
OR
- Detection of rubella virus by NAAT (e.g., throat, urine, blood or specimen from cataract) (NAAT for rubella is currently not available in Manitoba)
OR

a Characterized by fever and rash and at least one of the following: arthralgia/arthritis, lymphadenopathy or conjunctivitis (1).

b The most frequent reaction to measles-mumps-rubella (MMR) immunization is malaise and fever (with or without rash) occurring 7-12 days after immunization. However, this should be determined for each case, as these reactions and time frames can vary (1).

c IgM serology may be a false-positive. If the clinical presentation is inconsistent with a diagnosis of rubella or in the absence of recent travel/exposure history, IgM results must be confirmed by another listed confirmatory method. Rubella avidity serology is recommended for IgM positive results in pregnant women. Most acute rubella cases develop IgM after 5 days post rash onset. Therefore, a probable rubella case in which serum collected < 5 days after rash onset initially tests IgM negative should have a second serum collected > 5 days after onset for retesting for IgM.

- Positive serologic test for IgM antibody in the absence of recent immunization with rubella-containing vaccine
- OR
- Rubella IgG persisting beyond six months after birth (i.e., not from passive transfer of maternal antibody).

Still birth: Two clinically compatible manifestations (any combination from A and/or B below) with isolation of rubella virus from an appropriate clinical specimen (e.g., throat, urine, blood or specimen from cataract) (1).

A. Clinically Compatible Manifestations

- Cataracts or congenital glaucoma (either one or both count as one)
- Congenital heart defect
- Sensorineural hearing loss
- Pigmentary retinopathy

B. Clinically Compatible Manifestations

- Purpura
- Hepatosplenomegaly
- Microcephaly
- Micro-ophthalmia
- Mental retardation
- Meningoencephalitis
- Radiolucent bone disease
- Developmental or late onset conditions such as diabetes and progressive panencephalitis and any other conditions likely to be caused by rubella virus

1.22 Probable Case

In the absence of appropriate laboratory tests, a case that has at least:

- Any two clinically compatible manifestations listed under A above
- OR
- One manifestation listed under A above and one manifestation listed under B above.

NOTE: A case cannot generally be classified as confirmed CRS if:

- Rubella antibody titre is absent in the infant
- OR
- Rubella antibody titre is absent in the mother
- OR
- Rubella antibody titre declines in the infant consistent with the normal decline after birth of passively transferred maternal antibody (1).

1.3 Congenital Rubella Infection (CRI)

1.31 Confirmed Case

Laboratory confirmation of infection but with no clinically compatible manifestations. Laboratory confirmation includes at least one of:

- Isolation of rubella virus from an appropriate clinical specimen (e.g., nasal or throat swab, blood, urine, cerebrospinal fluid)
- OR
- Detection of rubella virus by NAAT (e.g., throat, urine, blood) (NAAT for rubella is currently not available in Manitoba)
- OR
- Positive serologic test for rubella IgM antibody in the absence of recent immunization with rubella-containing vaccine
- OR
- Rubella IgG persisting beyond six months after birth (i.e., not from passive transfer of maternal antibody) (1).

2. Reporting and Other Requirements

Laboratory:

- All positive laboratory results should be faxed (204-948-3044 secure fax) to

Manitoba Health, Public Health Surveillance Unit.

- Operators of Manitoba clinical laboratories are required to submit to Cadham Provincial Laboratory (CPL) within seven days of report the residual serum, plasma, respiratory specimens or respiratory viral isolate sub-cultures from individuals who tested positive for rubella.

Health Care Professional:

The completed reporting form (available at: www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf) should be faxed (204-948-3044 secure fax) to Manitoba Health, Public Health Surveillance Unit when a health professional becomes aware that a person meets or has recently met the probable or confirmed case definition for rubella or congenital rubella syndrome/infection.

3. Clinical Presentation/Natural History

Rubella: Clinical infection is usually mild, characterized by a generalized erythematous maculopapular rash, lymphadenopathy and slight fever (2). Up to 50% of infections are subclinical (3-4). Signs and symptoms are non-specific; rubella may be mistaken for other rash infections such as measles, dengue, parvovirus, adenoviruses, enteroviruses or human herpesvirus 6 (4-5). In children, a prodrome is rare and rash is usually the first manifestation (3). In older children and adults, there is often a one to five day prodrome with low-grade fever, malaise, lymphadenopathy and upper respiratory symptoms preceding the rash (3). The rash starts on the face, becomes generalized within 24 hours, and lasts approximately three days (2). Lymphadenopathy commonly involves the postauricular, posterior cervical and suboccipital nodes and lasts five to eight days (2-3). Adult infection is often accompanied by transient polyarthralgia or polyarthritis (4), especially in females (2). Complications are uncommon, but encephalitis (1:5,000 cases) and thrombocytopenia (1:3,000 cases) may occur (2). Symptomatic or asymptomatic rubella infection in pregnancy may lead to miscarriage, stillbirth, premature delivery or

fetal abnormalities (refer to “Congenital Rubella Syndrome” below) (3-4).

Despite the presence of specific immunity to rubella virus, reinfection with rubella virus may rarely occur (6-7).

Congenital Rubella Syndrome (CRS): In general, the younger the fetus when infected, the more severe the illness (6). Congenital malformations and fetal death may occur following inapparent maternal rubella infection (5). The most commonly described abnormalities associated with CRS are ophthalmologic (cataracts, pigmentary retinopathy, microphthalmos and congenital glaucoma), cardiac (patent ductus arteriosus, peripheral pulmonary artery stenosis), auditory (sensorineural hearing impairment), and neurologic (behavioral disorders, meningoencephalitis and mental retardation) (2). Neonatal manifestations of CRS include growth retardation, interstitial pneumonitis, radiolucent bone disease, hepatosplenomegaly, thrombocytopenia and dermal erythrocytosis (so called “blueberry muffin” lesions) (2). Moderate and severe CRS is usually recognizable at birth (5). Infants with mild CRS may appear normal at birth with abnormalities not being detected until months or years after birth (3, 5).

4. Etiology

Rubella is an enveloped RNA virus belonging to the genus *Rubivirus*, family *Togaviridae* (2, 5).

5. Epidemiology

5.1 Reservoir and Source

Humans (5).

5.2 Transmission

Rubella is transmitted primarily through direct or droplet contact from nasopharyngeal secretions of infected individuals (2). Congenital rubella syndrome occurs through transplacental infection of the fetus during the mother’s viremia (3). Infants with CRS shed large quantities of virus in their pharyngeal secretions and urine for a prolonged time, and may be a source of infection to their contacts (5).

5.3 Occurrence:

General: Rubella remains endemic in countries where rubella vaccine has not been introduced (5). In temperate areas, incidence is usually highest in late winter and early spring (3). In many countries, universal immunization has greatly reduced or practically eliminated rubella and CRS (5).

Canada: Following the introduction of routine infant immunization programs for MMR across Canada in 1983, the average number of reported rubella cases decreased from approximately 5,300 per year (1971 to 1982) to less than 30 cases per year (1998 to 2004) (8). Further, following the introduction of two-dose MMR schedules introduced in 1996-1997, the average incidence of rubella decreased from 0.08 per 100,000 in 1999 to 0.03 per 100,000 in 2004 (range 0.03 to 0.09 per 100,000), and the previously observed peaks in incidence have become less apparent (8). From 2000 to 2004, no more than three cases of CRS were reported each year in Canada (4). Since the late 1990s, rubella outbreaks have largely been restricted to isolated clusters of unimmunized individuals, including those who decline immunization for religious or philosophical reasons (4). Rubella virus continues to be introduced into the community by travellers (9).

Manitoba: In 1997, a large outbreak occurred affecting mostly non-immunized males aged 15 to 24 years. This was attributed to gaps in vaccination coverage that resulted from early selective immunization programs targeting pre-adolescent females in some jurisdictions (8, 10). One case of rubella was reported in 2007 and two cases in 2009. From 1991 to 2009, only three cases of congenital rubella were reported—two in 1993 and one in 1998.

5.4 Incubation Period

The incubation period for rubella is usually 16 to 18 days (2), but ranges from 14 to 23 days (2, 3).

5.5 Host Susceptibility and Resistance

Immunity is usually permanent after natural infection and believed to be long-term after immunization with rubella-containing vaccine (5).

However, persistent immunity may require contact with endemic cases (5). Infants born to immune mothers are usually protected for six to nine months after birth (5).

5.6 Period of Communicability

For rubella, communicability is from seven days before to seven days after onset of rash (2, 3, 5, 11, 12). Infants with CRS may continue to shed virus in nasopharyngeal secretions and urine for one year or longer and may transmit infection to susceptible contacts (2).

6. Laboratory Diagnosis

Clinical diagnosis of rubella is often inaccurate. Therefore, laboratory confirmation of infection should be attempted for all sporadic cases. All laboratory specimens should record date of onset of both fever and rash and date of collection.

6.1 Rubella

6.1.1 Serology

Generally rubella IgM is used for detection of acute cases and rubella IgG for immune status testing. A diagnosis of acute infection may be made on a single blood positive for rubella IgM in the absence of recent immunization. However, rubella IgM serology may have false-positives. If the clinical presentation is not consistent with a diagnosis of rubella or in the absence of recent travel/exposure history, rubella IgM results must be confirmed by another method listed in section 1.1.1 for “Confirmed Case.”

Most rubella cases develop IgM antibody five days after rash onset. Therefore, a suspected rubella case in which serum collected less than five days after rash onset initially tests IgM negative should have a second serum collected greater than five days after rash onset for IgM retesting.

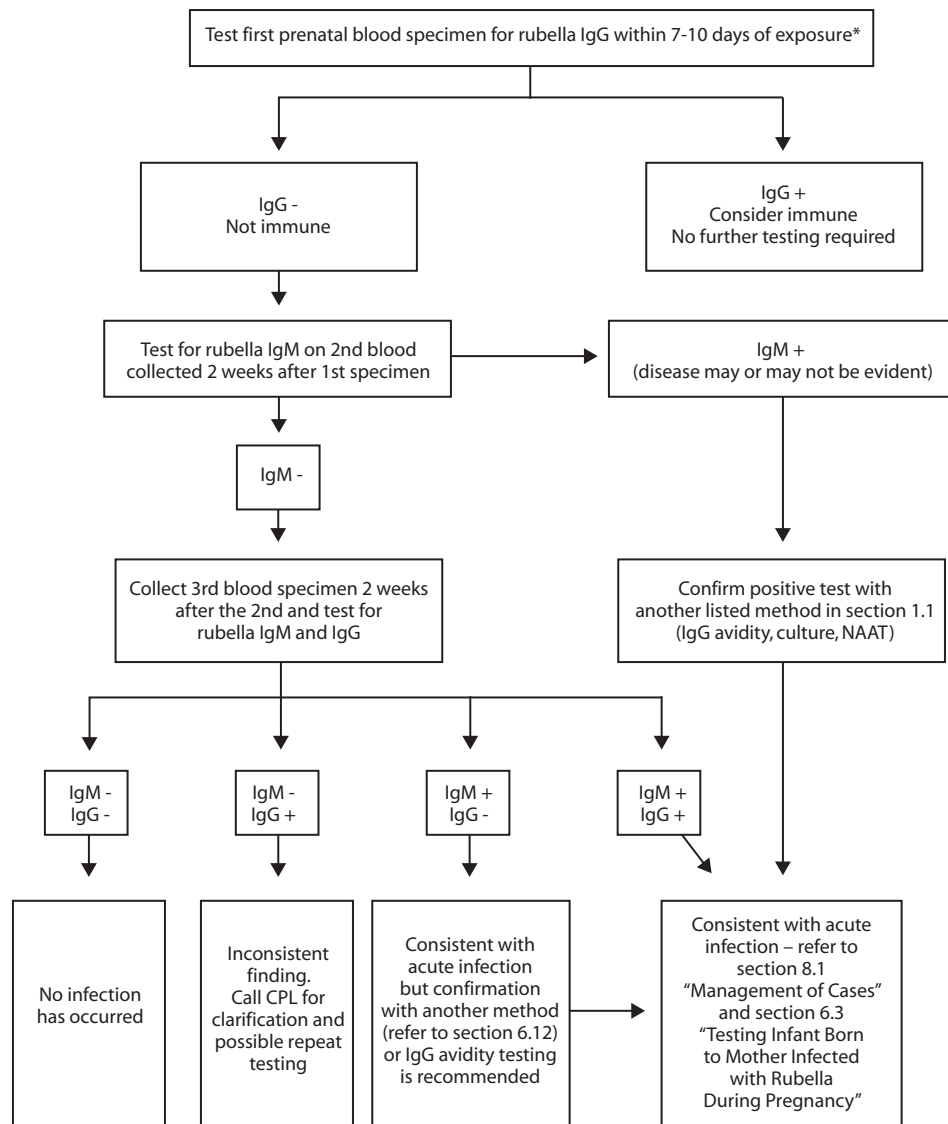
6.1.2 Virus Detection

Available upon request for sporadic rubella cases. Cadham Provincial Laboratory (CPL) virology section (204-945-6123, after hours: 204-945-6655) should be consulted prior to sending specimens for virus

detection. Rubella nucleic acid amplification test (NAAT) is currently not available in Manitoba. A nasal or throat swab should be collected with a Dacron or rayon-tipped swab and placed in viral transport medium. All specimens should be transported with a

cold pack (to maintain a temperature of approximately 4°C) to CPL as soon as possible. Alternatively, 15-20 ml of urine or products of conception should be collected and placed in a sterile container.

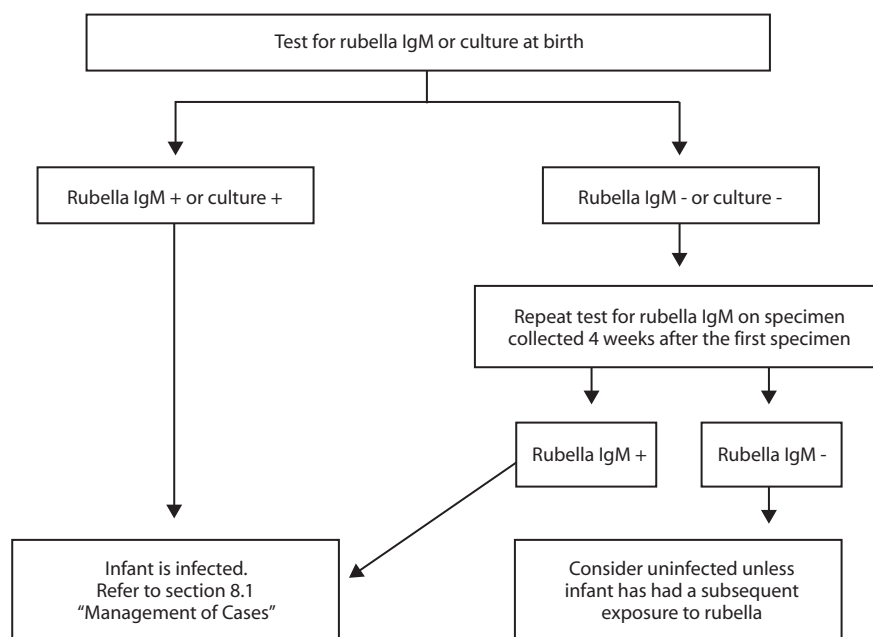
6.2 Testing Pregnant Women Who Have Been Exposed to Rubella⁺



⁺ If symptoms consistent with acute rubella develop after a known or suspected exposure to rubella, viral detection as per section 6.12 is indicated.

^{*} Delaying specimen collection beyond 7-10 days of the exposure may make distinguishing between IgG positivity due to recent or current exposure/infection and IgG positivity due to past infection/immunity more difficult. For exposures that occurred > 10 days prior, consult CPL for appropriate testing plan.

6.3 Testing Infant Born to Mother Infected with Rubella During Pregnancy (Congenital Rubella Syndrome/Infection)



Clinical manifestation and history of exposure are critical for the diagnosis of rubella infection in an infant born to a probable infected mother. Rubella infection in newborn infants is diagnosed by virus isolation or by the detection of rubella IgM antibody in the blood of the newborn. Cord blood is not acceptable. Detection of rubella IgG antibody is not recommended for the diagnosis of newborn infant infection.

7. Key Information for Public Health Response

- Immunization history including date(s) and type of vaccine if known.
- Recent exposure/travel history of cases (e.g., 14-23 days before rash onset).
- Identification and appropriate follow-up of susceptible contacts (refer to "Management of Contacts" below).

8. Control

8.1 Management of Cases

Reported cases are referred to their Regional Health Authority (RHA) of residence or First Nations Inuit Health (if applicable) for follow-up. Cases should be interviewed for contacts and any known pregnant contacts should receive immediate follow-up (refer to "Management of Contacts" below).

All rubella cases should be advised to practice good hand hygiene, avoid sharing drinking glasses or utensils, and cover coughs and sneezes with a tissue or forearm.

Cases who are health care workers (HCWs) should be advised to immediately notify Occupational Health and Infection Prevention and Control for the facility/regional program in which they work and in consultation with them determine when it is appropriate to return to work. Because of the mode of transmission of rubella, any cases who are

HCWs, including community workers and support staff may pose a threat to their work place.

Congenital rubella syndrome/infection (CRS/CRI) cases should be monitored for the development of clinical manifestations. Appropriate expert consultation should be sought.

Treatment:

- Supportive, no specific treatment is available.

Public Health Measures:

Rubella:

- Hospitalized patients with rubella should be managed with Droplet Precautions in addition to Routine Practices until seven days after rash onset. Refer to *Infection Control Guidelines: Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Health Care. Canada Communicable Disease Report CCDR, 1999: 25S4: 1-142.*
- Rubella cases should be excluded from school, day care, work and sporting events for seven days after rash onset (2, 5, 12).
- Rubella cases should avoid contact with pregnant females and any known pregnant contacts should be followed up as per “Management of Contacts” below.

Congenital Rubella Syndrome/Infection:

- Hospitalized infants with CRS/CRI should be managed with Droplet and Contact Precautions (in addition to Routine Practices) until they are at least 12 months of age unless two consecutive nasopharyngeal and urine culture specimens collected after three months of age are negative for rubella virus (2).
- All individuals who have contact with a child with CRS/CRI (e.g., care givers, household and day care contacts, medical personnel, laboratory workers) should be immune^d to rubella (13).

- Pregnant females should avoid contact with CRS/CRI cases. Any known pregnant contacts should be followed up as per “Management of Contacts” below.

Special Considerations for Management of Infected Pregnant Women:

- The time of infection should be established as the effects of congenital rubella syndrome vary with time of gestation (14).
- Pregnant women should be counselled about the possible risk of vertical transmission and the effects on the fetus. The option of pregnancy termination, especially if primary infection occurs prior to 16 weeks gestation should be discussed (14).
- Immune globulin (Ig) is not recommended for pregnant women with acute infection as there is no evidence that it ameliorates fetal infection (14).
- Infected pregnant women should be referred to the Clinical Genetics Department at the Health Sciences Centre (204-787-4631), and subsequently, if appropriate, to the Fetal Assessment Unit, Women’s Hospital.

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- d A person is considered immune to rubella if any of the following apply:
- Record of prior immunization with at least one dose of rubella-containing vaccine.
 - Documented history of laboratory-confirmed rubella infection.
 - Immunity to rubella documented by a recent rubella IgG positive/protective titre.

8.2 Management of Contacts

The Regional Health Authority of case residence or First Nations Inuit Health (if applicable) will contact reported cases to establish a list of exposed persons and identify susceptible contacts. Contacts who are pregnant should receive priority for follow-up. Examples of exposure situations where contacts should be identified include home, child care facility, school, school bus, workplace, physician office and hospital emergency department. Airline passengers who have been exposed to a confirmed rubella case on the same flight should be considered, if feasible, for notification of exposure, assessment of immune status, and recommendation for vaccination if the flight occurred in the past two weeks (15).

Definition of Contact: Someone with unprotected exposure within two metres of a case during the communicable period—seven days before onset of rash until seven days after onset of rash (16). Persons with more prolonged contact will have an increased risk for infection.

Definition of Susceptible Contact: A contact (defined above) who does not meet any of the following (4):

- Record of prior immunization with at least one dose of rubella-containing vaccine.
- Documented history of laboratory-confirmed rubella infection.
- Immunity to rubella documented by a recent rubella IgG positive/protective titre.

A contact is considered rubella immune if any of the above criteria apply.

8.21 Recommendations for Management of Contacts

Susceptible contacts, as defined above, who are ≥ 12 months of age AND do not have contraindications to rubella-containing vaccine (e.g., immunocompromised, pregnant, allergy to vaccine component) should be immunized with

one dose of measles-mumps-rubella (MMR^e) vaccine as soon as possible. Although immunization will not prevent infection after exposure to wild-type rubella virus, it is not harmful and will provide future protection (4). One dose of rubella-containing vaccine is currently recommended for protection against rubella. Refer to the current *Canadian Immunization Guide* and supplemental statements from the National Advisory Committee on Immunization (NACI). Refer also to the vaccine product monograph for information on clinical use. Women of childbearing age should be advised to avoid pregnancy for one month after immunization (4).

Contacts should be counselled regarding the signs and symptoms of rubella and the need to report to their health care provider should these develop. Symptomatic contacts should be instructed to call before presenting to a health care provider to limit potential transmission to susceptible individuals in the health care setting. Contacts should be encouraged to practice good hand hygiene, avoid sharing drinking glasses or utensils and cover coughs and sneezes with a tissue or forearm.

Contacts who are health care workers should be advised to notify Occupational Health and/or Infection Prevention and Control for the facility/regional program in which they work and in consultation with them determine when it is appropriate to return to work.

8.22 Recommendations for Management of Contacts who are Pregnant

Pregnant contacts should be advised to consult with their physician promptly. The physician should confirm rubella susceptibility status (refer to section 6.2 “Testing Pregnant Women who have been Exposed to Rubella”). Refer to “Management of Cases” above if contact is found to be infected.

^e In Canada, rubella-containing vaccine is only available in combination with the measles and mumps vaccine (MMR).

In the event of maternal exposure early in pregnancy (< 16 weeks), immune globulin (Ig) may modify or suppress symptoms in the pregnant woman but does not uniformly prevent infection, including congenital infection (4). Therefore, the routine use of Ig in susceptible women exposed to rubella early in pregnancy is not recommended (4). Large volume Ig (20 mL) should only be considered when a pregnant woman exposed to rubella would not consider termination of pregnancy (17). If Ig is a consideration, contact your local Medical Officer of Health (MOH) or the MOH on call (204-788-8666). Consultation with a medical specialist is also strongly recommended.

8.3 Management of Outbreaks:

Outbreak control is important for preventing CRS/CRI.

Definition of Outbreak: Confirmed cases in excess of what is expected in the jurisdiction over a given period of time.

- Public notification to identify and protect susceptible pregnant women (5): the level of notification will be at the discretion of Regional Public Health and/or the Office of Disaster Management.
- During rubella outbreaks, susceptible individuals (i.e., those who have not received any doses of rubella-containing vaccine and who have no serologic proof of immunity) should be given one dose of rubella-containing vaccine (MMR) promptly without prior serologic testing, unless contraindicated (4). Although immunization will not prevent infection after exposure to wild-type rubella virus, it is not harmful and will provide future protection (4). Immunization will also provide protection against measles and mumps (4).

8.4 Preventive Measures:

- Prompt identification and management of cases and contacts.

- Routine two-dose immunization of all children at one year and at four to six years of age (preschool) with MMR (measles-mumps-rubella) vaccine. Although only one dose of rubella-containing vaccine is currently recommended for children, the second dose is a convenience dose, required for protection against measles (4) and mumps (18). MMR vaccine is the only rubella-containing vaccine currently available in Canada.
- One dose of rubella-containing vaccine (MMR) is recommended for all adolescents and adults unless they have proof of immunity, either a record of prior immunization with at least one dose of rubella-containing vaccine, a documented history of laboratory-confirmed rubella disease, or serological proof of immunity (4).
- In schools and other educational institutions, exclusion of persons without valid evidence of immunity in outbreak settings may:
 - limit disease transmission and
 - help to raise the vaccination level in the target population as individuals may prefer vaccination if exclusion is the only alternative (19).
- Review of the rubella vaccine status of persons planning travel to rubella-endemic countries and immunization if not immune (4).
- Recognition and immunization of any non-pregnant woman of childbearing age without a history of previous immunization or serologic immunity whenever an opportunity presents. Women of childbearing age should be advised to avoid pregnancy for one month after immunization (4).
- Offering MMR vaccine to immigrant women from developing countries at their

first encounter with the health care system (11, 20), unless:

- Already pregnant;
- Proof of past immunization with rubella-containing vaccine (i.e., immunization record);
- Have documented immunity (9).

Waiting for results of serologic screening may result in a missed opportunity to vaccinate (20).

- Routine screening of all prenatal bloods for protective levels of antibody and postpartum immunization in hospital of all women found to be susceptible.
 - For susceptible women who are not immunized in hospital (as identified on the postpartum referral), it is recommended that the public health nurse inform the postpartum client of the importance of receiving one dose of MMR vaccine from a health care provider as soon as possible (for example, at the postnatal visit with their primary care provider, at a visit when the infant receives an immunization, or with the public health nurse at a community clinic).
 - Routine screening for rubella antibodies either after immunization or in subsequent pregnancies is not recommended as protection against CRS is likely after immunization (4).
 - Those with a prior record of immunization with at least one dose of rubella-containing vaccine who are found to be non-immune serologically through the routine rubella prenatal screening program do not require repeat immunization as they are likely protected against CRS (4).
- Advise rubella-susceptible pregnant women to avoid persons with rubella and congenital rubella syndrome/infection

and to report any contacts with cases to their physician immediately (16).

- Given that maternal infection (i.e., re-infection) can occur even after vaccination or documented immunity (7, 21), contact with rubella should be avoided throughout the first two trimesters of pregnancy even in “IgG-positive” pregnant women (7).

Note: Refer to the current *Canadian Immunization Guide* and supplemental statements from the National Advisory Committee on Immunization (NACI) for additional information on immunization with MMR vaccine. Refer also to the vaccine product monograph for information on clinical use.

Prevention in Health Care Workers:

- Exposed susceptible HCWs (i.e., who lack evidence of immunity) should be excluded from duty from the seventh day after the first exposure through the 21st day after their last exposure (12).
- Immunization of rubella-susceptible HCWs with MMR vaccine unless contraindicated (e.g., pregnant women) (12).

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