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No. 368-Rubella in Pregnancy

This Clinical Practice Guideline was prepared by the Infectious Diseases Committee, reviewed by the Guideline Management and Oversight Committee, and approved by the Board of the Society of Obstetricians and Gynaecologists of Canada

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Key Words: Rubella, congenital rubella syndrome, pregnancy, immunization

KEY MESSAGES

1. Prenatal screening is an opportunity to identify women susceptible to rubella and arrange for postpartum vaccination.
2. Women with 2 documented measles, mumps, rubella (MMR) vaccine doses or positive rubella immunoglobulin G do not need prenatal rubella screening, not even in future pregnancies.
3. Postpartum vaccination with measles, mumps, rubella (MMR) is contraindicated for women on systemic immunosuppression (i.e., biologics).
4. Consider delaying postpartum vaccination if any immunoglobulin products (i.e., RhoGAM or blood) were used in pregnancy.
5. Inadvertent rubella vaccination in early pregnancy is not an indication for pregnancy termination.

Abstract

Objective: To review the epidemiology, natural history, evaluation, and prevention of rubella infection during pregnancy. This will aid obstetric care providers in counseling their patients regarding potentially devastating effects on the developing fetus and the importance of vaccinating susceptible women as appropriate.

Outcomes: Outcomes evaluated include fetal rubella infection, maternal seroconversion and response to rubella-containing vaccines.

Evidence: Medline, PubMed, EMBASE, and Cochrane databases were searched for articles in English on subjects related to rubella infection during pregnancy betweenn 1985 and 2017. Results were restricted to systematic reviews, randomized controlled trials/controlled clinical trials, and observational studies. Other (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections,

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Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment[a]	Classification of recommendations[b]
I: Evidence obtained from at least 1 properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action.
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action.
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than 1 centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.	D. There is fair evidence to recommend against the clinical preventive action.
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action.
	L There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

[a] The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

[b] Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Adapted from: Woolf SH, et al. Assessing the clinical effectiveness of preventive maneuvers: analytic principles and systematic methods in reviewing evidence and developing clinical practice recommendations. A report by the Canadian Task Force on the Periodic Health Examination. J Clin Epidemiol 1990;43:891-905.

clinical trial registries, and national and international medical specialty societies.

Valuation methods: The quality of the evidence is rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1). Recommendations for practice are ranked according to the method described in this Report.

Guideline update: The guideline will be reviewed 5 years after publication to decide if an update is required. However, if important new evidence is published prior to the 5-year cycle, the review process may be accelerated for a more rapid update of some recommendations

Sponsor: Society of Obstetricians and Gynaecologists of Canada.

Recommendations:

1. Screening for rubella serostatus is recommended as part of standard prenatal screening if a pregnant woman has no record of rubella past immunity and no proof of immunization against rubella (III-B).
2. Since the effects of rubella infection in pregnancy vary with the gestational age at the time of infection, accurate gestational dating should be established, as well as timing of rubella infection, as they are critical to counselling (II-3A).
3. In a pregnant woman exposed to rubella or who develops signs or symptoms of rubella or whose fetus presents ultrasound anomalies compatible with congenital rubella syndrome, serological testing for rubella immunoglobulin M and immunoglobulin G should be performed to determine immune status and risk of congenital rubella syndrome (III-A).
4. Women should be counselled about the possible risk of vertical transmission and informed regarding the option of pregnancy termination, especially if primary infection occurs prior to 16 weeks gestation (III-A).
5. Rubella immunization should not be administered in pregnancy but may be safely given postpartum, as long as there is no contraindication to receive a live vaccine (i.e., systemic immunosuppression). Consider delaying vaccination if the woman received any immunoglobulin-containing preparations, including Rh immunoglobulin or intravenous immune globulin, or blood products during pregnancy or the peripartum period, as there is potential for reduced vaccine effectiveness (III-B).
6. Women who have been inadvertently vaccinated in early pregnancy or who become pregnant immediately following vaccination can be reassured that there have been no cases of congenital rubella syndrome documented in these situations (III-B).
7. Women wishing to conceive should be counselled and encouraged to have their rubella antibody status determined if no record of rubella past immunity and no proof of immunization are available and undergo rubella vaccination if needed (III-B).

INTRODUCTION

Rubella, also called German measles, is a disease of childhood that has markedly declined in incidence in North America since the introduction of routine childhood rubella vaccination. It is usually clinically manifested as a mild self-limited infection. During pregnancy, maternal infection can lead to miscarriage, stillbirth or CRS — a specific set of congenital anomalies including central nervous system damage like microcephaly, microphthalmia and other eye defects, sensorineural hearing loss, and heart defects.[1] Human beings are the only known host. This document reviews the implications and the management of rubella infection during pregnancy. Recommendations are evaluated using the evidence criteria of the Canadian Task Force on Preventive Health Care (Table 1).[2,3]

EPIDEMIOLOGY

In Canada, before the use of rubella-containing vaccine, rubella incidence was cyclical with large peaks seen every 3 to 6 years. After the rubella vaccination program was implemented in the 1970s, annual incidence declined markedly from 37 cases per 100 000 population in 1969-1973 to 6 cases per 100 000 population between 1984 and 1995. Similarly, CRS went from 3 annual cases per 100 000 live births between 1979 and 1983 to 0.8 cases per 100 000 live births in 1984-1997.[4] In 2005, over 300 cases of rubella were confirmed in southwestern Ontario in a community in which many members had not been vaccinated or had not accepted routinely recommended vaccines.[5] Fortunately, no CRS cases were reported as a result of this outbreak.[5] Since then, rubella and CRS have largely been eliminated in Canada; between 2006 and 2014, an average of 5 annual cases of rubella infection have been reported, all of them imported and of sporadic occurrence. Since 2000, no cases of CRS arising from infection acquired in Canada have been reported, and only 2 imported cases of CRS have been reported since 2006, both in infants born to women who immigrated and acquired rubella prior to arrival to Canada.[5]

According to the WHO, the WHO region of the Americas is free of endemic transmission of rubella since April 2015[6]; however, cases of CRS continue to occur in other parts of the world,[7] and unfortunately, the goal of elimination of rubella in the WHO European Region by 2015 was not reached.[8]

Approximately 90% (89% to 93%) of pregnant women in Canada are immune to rubella based on routine prenatal testing. Susceptibility is higher among young Canadian-born women, women living in certain geographic locations (e.g., northern Alberta and northern Ontario), and new immigrant pregnant women.[9–11] Prenatal testing provides an opportunity to identify women susceptible to rubella and to arrange for postpartum immunization if there is no record of rubella past immunity and no proof of immunization against rubella.

Recommendation

1. Screening for rubella serostatus is recommended as part of standard prenatal screening if a pregnant woman has no record of rubella past immunity and no proof of immunization against rubella (III-B).

CLINICAL MANIFESTATIONS

Rubella is usually characterized by a mild, self-limited disease associated with a characteristic rash.[2] The incubation period is 12–23 days, followed by an infectious period ranging from 7 days before to 5–7 days after rash onset.[2] Although rubella is asymptomatic in 25% to 50% of cases, some individuals may experience mild prodromal symptoms such as low-grade fever, conjunctivitis, sore throat, coryza, headaches or malaise, and tender lymphadenopathy. These prodromal symptoms will usually last 1 to 5 days before the onset of the scarletiniform rash (innumerable small red papules that are widely and diffusely distributed), which may be mildly pruritic.[12] The rash characteristically begins on the face and spreads to the trunk and extremities. It will usually resolve within 3 days in the same order in which it appeared (face first and then body).

Polyarthritis and polyarthralgia can develop 1 week after the rash, mostly in adolescent and adult women (60% to 70%).[13] Classically, hands, knees, wrists, and ankles are affected symmetrically for 1 to 4 weeks. Other manifestations, although rare, include tenosynovitis, carpal tunnel syndrome, thrombocytopenia, post-infectious encephalitis, myocarditis, hepatitis, hemolytic anemia, and hemolytic uremic syndrome.[14,15]

ABBREVIATIONS

CRS	congenital rubella syndrome
CVS	chorionic villus sampling
IgG	immunoglobulin G
IgM	immunoglobulin M
IVIG	intravenous immune globulin
MMR	measles, mumps, rubella
MMRV	measles, mumps, rubella, varicella
NAAT	nucleic acid amplification techniques
PCR	polymerase chain reaction
WHO	World Health Organization

It is important to remember that rubella's clinical presentation is non-specific. Other infections can present with a nonvesicular rash, such as parvovirus B19, measles, human herpesviruses (HHV 6 and 7) and enteroviruses. Parvovirus B19 and arbovirus (dengue, Chikungunya, West Nile, and Zika) infections are also associated with rash and joint symptoms. Therefore, consideration should be made to investigate pregnant women for other infections if rubella infection is clinically suspected.

Infection during pregnancy can result in CRS (described in the following section), spontaneous abortion and stillbirth.[16]

CONGENITAL RUBELLA SYNDROME

CRS represents the manifestations of congenital infection with the rubella virus. The infection affects many fetal systems.[1,17,18] The most common congenital defects and late manifestations are shown in Table 2.[18–21]

Many children born with CRS will demonstrate persistent neuromotor deficits later in life.

INTRAUTERINE TRANSMISSION AND RISK OF CONGENITAL RUBELLA SYNDROME

Fetal infection is acquired hematogenously, and the rate of transmission varies with the gestational age at which maternal infection occurs (Figure 1). After infecting the placenta, the rubella virus spreads through the vascular system of the developing fetus, causing cytopathic damage to blood vessels and ischemia in developing organs.[17,22–27] Spontaneous abortion may occur in up to 20% of cases when rubella occurs in the first 8 weeks of pregnancy.

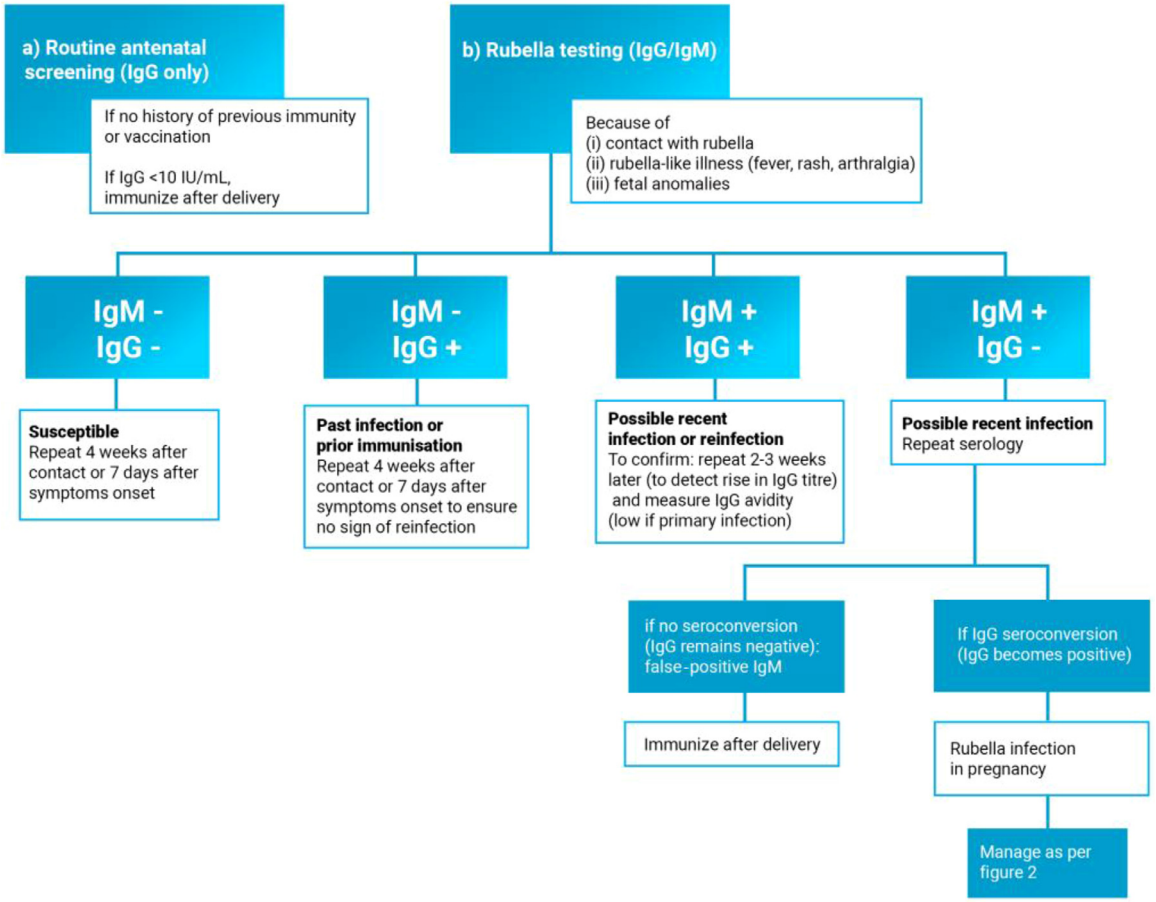
The risk of CRS after maternal infection is essentially limited to the first 16 weeks of gestation. Risk of CRS is 65% to 85% in the first 2 months of gestational age, decreasing to 30% to 35% and single organ involvement (deafness or congenital heart disease) for infections in the third month of gestation and only 10% for the fourth month.[28] Little, if any, risk of CRS is associated with infection beyond 20 weeks, and intrauterine growth restriction seems to be the only sequela of third trimester infections.[13–19,23,27,29] Periconceptional maternal infection does not seem to increase the risk of CRS.[25]

Maternal immunity, either from vaccination or natural infection, is generally protective against intrauterine rubella infection.[30,31] However, there have been cases of CRS with maternal reinfection, all limited to <12 weeks of gestational age,[32] among both women with either natural or acquired immunity.[4,30–37] Therefore, CRS should always be considered in a fetus or neonate with ultrasound findings or clinical picture suggestive of congenital infection regardless of maternal serostatus.

Table 2. Prenatal ultrasound findings, presentation at birth, and late manifestations of CRS[18–21]

Prenatal ultrasound findings	Congenital rubella syndrome at birth	Late manifestations
Cardiac	Cardiac defects (10%–20%)	Endocrine
Septal defects	Pulmonary stenosis	Diabetes mellitus
Pulmonary artery stenosis	Patent ductus arteriosus	Thyroiditis
Cerebral	Central nervous system (10%–25%)	Growth hormone deficit
Microcephaly	Microcephaly	Neurodevelopmental
Ventriculomegaly	Meningoencephalitis	Progressive panencephalitis
Periventricular calcifications	Sensorineural deafness (19%)	Mental retardation
Ocular	Ophthalmic defects (10–25%)	Behavioral disorder
Microphthalmia	Retinopathy	Autism
Cataracts	Chorioretinitis	
Other	Cataracts	
Intrauterine growth restriction	Microphthalmia	
Amniotic fluid abnormalities	Pigmentary and congenital glaucoma	
Hepatosplenomegaly	Others	
	Thrombocytopenia	
	Hepatosplenomegaly	
	Jaundice	
	Radiolucent bone disease	
	Purpura	

Figure 1. Diagnosis of suspected maternal rubella infection.[17,22–27]



Recommendation

2. Since the effects of rubella infection in pregnancy vary with the gestational age at the time of infection, accurate gestational dating should be established, as well as timing of rubella infection, as they are critical to counselling.

DIAGNOSIS OF RUBELLA INFECTION

Diagnosis of Maternal Infection

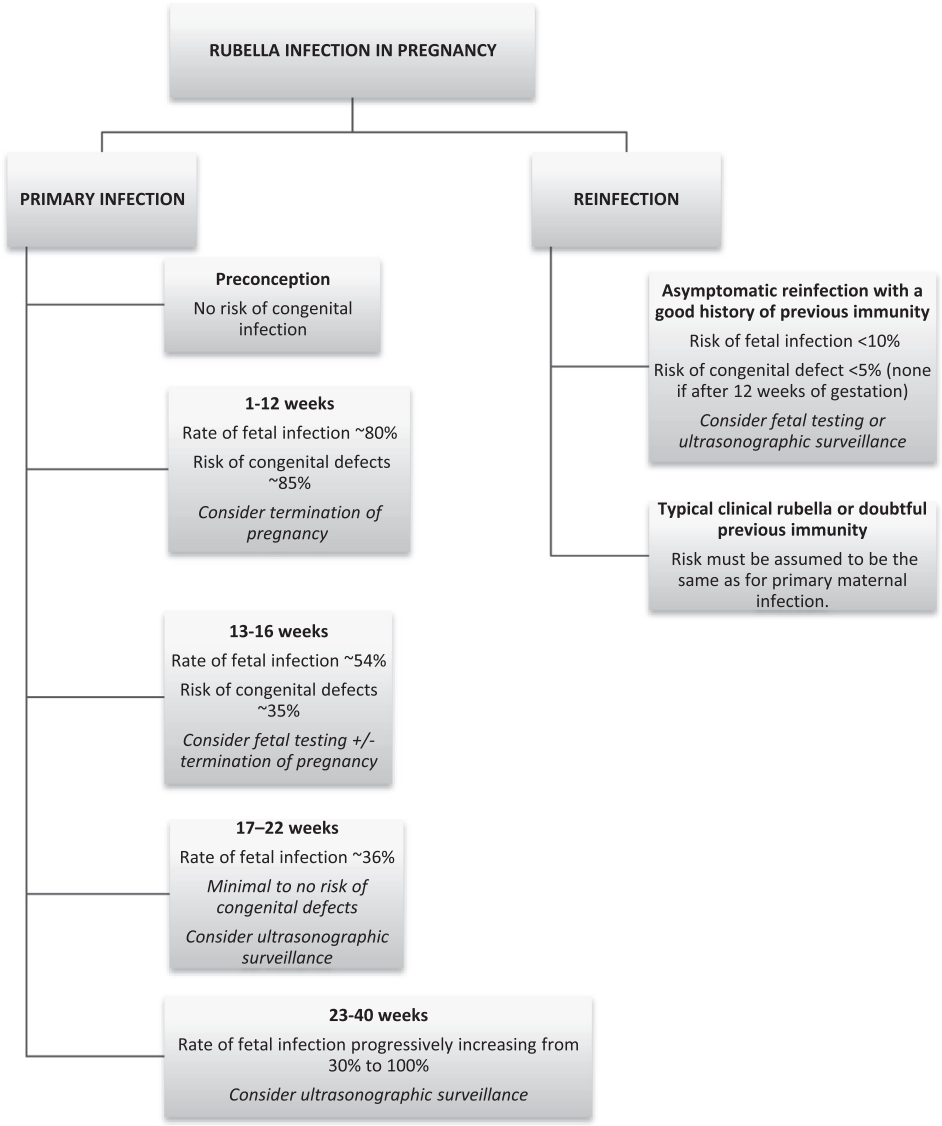
Accurate diagnosis of rubella infection in pregnancy is crucial and requires determination of maternal serostatus, since an important number of cases (about 50%) are subclinical. Serology by enzyme-linked immunosorbent assay to measure rubella-specific IgG and IgM titres is widely available. IgG avidity helps to differentiate primary or recurrent infections: low IgG avidity indicates recent infection, whereas high avidity index means past infection or immunization.[38–41] NAAT and PCR are useful to confirm rubella infection when IgM test results are equivocal and for surveillance of circulating genotypes. Nasopharyngeal and throat specimens are the ideal samples if collected in the first 5 days after the rash onset.[38] In addition, viral cultures drawn from nasal, blood, throat, urine, or cerebrospinal fluid may be positive from 1 week before to 2 weeks after the onset of the rash.[2,42] Figure 2 describes the interpretation of serological tests.

Recent rubella infection is defined as[22]:

- A 4-fold rise in rubella IgG antibody titres between acute and convalescent serum specimens
- Rubella-specific IgG seroconversion OR
- A positive serological test result for rubella-specific IgM antibody and low-avidity IgG OR
- A positive rubella culture or viral detection via reverse-transcription PCR

Timing of laboratory testing is important for rubella diagnosis, since it is a mild disease of short duration and interpretation depends on the time of sample collection relative to the onset of symptoms.[38,43] Serological studies are best performed within 7 to 10 days after the onset of the rash and should be repeated 2 to 3 weeks later (i.e., acute and convalescent).

Figure 2. Risk of CRS according to timing and type of rubella infection in pregnancy and preconception, and suggested antenatal management.



Even though a positive rubella-IgM result in the right clinical context was traditionally confirmatory of acute infection, positive rubella-IgM antibodies in pregnancy should be interpreted with caution, as false positives occur and occasionally rubella-specific IgM antibodies may persist for months or years after infection or vaccination. Since false-positive results are becoming relatively more frequent as rubella incidence declines, it is important that a positive rubella-IgM result in a pregnant woman is thoroughly investigated using other confirmatory tests such as paired IgG (acute and convalescent), IgG avidity,[38–41] or rubella virus isolation by culture or NAAT,[22,38] to avoid unnecessary terminations of pregnancy.

Recommendation

3. In a pregnant woman who is exposed to rubella or who develops signs or symptoms of rubella or whose fetus presents ultrasound-detected anomalies compatible with congenital rubella syndrome, serological testing for rubella immunoglobulin M and immunoglobulin G should be performed to determine immune status and risk of congenital rubella syndrome (III-A).
4. Women should be counselled about the possible risk of vertical transmission and informed regarding the option of pregnancy termination, especially if primary infection occurs prior to 16 weeks gestation.

Diagnosis of Fetal Infection

There is no gold standard for antenatal diagnosis of rubella congenital infection. Rubella PCR, rubella culture, and fetal IgM can be performed following CVS, fetal blood sampling, or amniocentesis.[22,44-49] Amniocentesis is recommended at least 6 weeks after known maternal infection and after the 20th week of gestation. Prenatal tests need to be interpreted with caution: CVS has been associated with contamination with maternal tissue resulting on false-positive PCR, and false negative-fetal IgM is common until late in pregnancy.

Common ultrasound findings most frequently associated with CRS are listed in Table 2. None of these findings is specific for rubella; hence, any fetus presenting with these should be evaluated for congenital viral infections, including rubella.[14]

MANAGEMENT OF RUBELLA INFECTION IN PREGNANT WOMEN

The management of the exposed pregnant woman must be individualized and depends on the timing of pregnant patient's rubella infection and rubella immunity. Suggested management is provided in Figure 1.

TREATMENT

Treatment of acute rubella infection is supportive. The prognosis is generally excellent for pregnant women with rubella infection.

A 2015 Cochrane collaboration systematic review[50] supports postexposure prophylaxis with intramuscular or intravenous infusion of rubella-specific immunoglobulin for the prevention of rubella infection among exposed pregnant women up to 5 days after exposure, with a number needed to treat of 4; however, there is insufficient evidence to know whether this strategy prevents CRS.

RUBELLA VACCINATION

The first live attenuated rubella vaccine was introduced in 1969. A single dose of this vaccine will result in measurable antibody in almost 95% of susceptible persons; primary failure of the rubella vaccine occurs in less than 5% of immunizations.[51] Antibody levels can be detected for at least 18 years in more than 90% of the vaccine recipients[7]; however, up to 20% of vaccinated individuals will have rubella titres below the protective level after 2 decades from immunization,[52] and some individuals will not mount an immune response that produces protective levels of rubella IgG as detected by routine assays. Immune studies of these individuals following a booster dose of the rubella vaccine demonstrate an immune response consistent with prior immunity,[53,54] and up to 50% of them have evidence of cellular immunity that can provide adequate protection against rubella infection.[55] Although rubella infection may occur in immunized pregnant women, these reinfections result in only 8% risk of CRS in the first trimester of pregnancy[30] compared with a risk of 65% to 85% among patients without any immunity.[28]

The occurrence of "non-protective" antibody levels despite adequate immunization with rubella-containing vaccines is an issue in countries like Canada that have achieved elimination, as lack of circulating rubella wild-type virus decreases the detectable rubella IgG levels among cohorts of women who were born after universal vaccination became available.[56] In Canada, 1 dose of rubella-containing vaccine is recommended at 12 to 15 months of age, using either MMR or MMRV vaccines. Even though a single dose of these vaccines is all that is required for rubella protection, 2 doses of measles, mumps, and varicella–containing vaccines are required for protection against these other infections. The second dose is recommended at 18 months of age or any time thereafter, but no later than school entry. A large proportion of women born in Canada after the universal MMR immunization program was implemented in 1983 have received 2 doses of MMR, but up to 37.7% to 47.2% of them have rubella IgG antibodies below what is considered a protective level,[56] highlighting the fact that antibody level cutoffs that were determined when wild-type rubella virus was circulating may no longer be appropriate in countries like Canada.

The rubella vaccine is usually well tolerated. Side effects to vaccination, although rare, include arthritis, arthralgia, rash, adenopathy, and fever.[51] The actual vaccine-related frequency of acute arthritis or arthralgia in non-immune women is in the order of 5% each. However, there is no evidence of any increased risk of new onset chronic arthropathies or neurological conditions in women receiving the RA27/3 rubella vaccine. There are no epidemiological data supporting an association of CRS or autism with the MMR vaccine.[57]

Contraindications to rubella vaccinations include febrile illness, certain immunodeficiencies and systemic immunosuppression, history of an anaphylactic reaction to neomycin, and pregnancy.[2] Rubella vaccine virus has the potential to cross the placenta and infect the fetus.[2] However, there has been no report of CRS in the offspring of women inadvertently vaccinated during early pregnancy.[58,59] Therefore, pregnancy termination is not recommended for these patients.[60] Given the potential risks to

the fetus, women are advised not to become pregnant for a period of 28 days after immunization.[61]

The vaccine can be given safely to postpartum women who are breastfeeding and to the children of pregnant women, since infection is not transmitted from recently immunized individuals.[7] However, it should be noted that postpartum vaccination with MMR is contraindicated for women receiving systemic immunosuppression with biologics like anti–tumour necrosis factor agents or long term high-dose steroid treatment (prednisone equivalent of ≥ 20 mg/day for ≥ 14 days).

Another consideration is to delay postpartum vaccination if the patient received any immunoglobulin-containing preparations, including Rh immune globulin, IVIG, or blood products, during pregnancy or the peripartum period, as vaccine effectiveness may be reduced. The recommended interval between receipt of Rh immune globulin or blood products and subsequent administration of MMR or MMRV will typically vary between 3 and 6 months, but it may need to be as long as 11 months for women who received large doses of IVIG. For more information see Table 3 (adapted from the Canadian Immunization Guide).[62] If there is a need to vaccinate a postpartum woman without delay, such as in cases of recent exposure to rubella, risk of pregnancy within 3 months postpartum, or potential loss to follow-up, the vaccination should still be given before hospital discharge, but serological testing to confirm immunity is recommended.

Recommendations

5. Rubella immunization should not be administered in pregnancy but may be safely given postpartum, as long as there is no contraindication to receive a live vaccine (i.e., systemic immunosuppression). Consider delaying vaccination if the patient received any immunoglobulin-containing preparations, including Rh immune globulin, intravenous immunoglobulin or blood products during pregnancy or the peripartum period, as there is potential for reduced vaccine effectiveness (III-B).
6. Women who have been inadvertently vaccinated in early pregnancy or who become pregnant immediately following vaccination can be reassured that there have been no cases of congenital rubella syndrome documented in these situations (III-B).

PREVENTION

The best therapy for CRS is prevention. In fact, the main reason for vaccination against rubella is to prevent infection during pregnancy. To prevent CRS, the following steps are recommended.

1. Providing universal infant immunization to decrease circulation of rubella virus (instituted in all Canadian provinces and territories in 1983).
2. Using MMR or measles-rubella vaccine as the immunizing agent in catch-up campaigns and as the second dose in the new 2-dose routine immunization program for measles.
3. Ensuring that girls are immune before they reach child-bearing age and using every opportunity to assess the immunity of women of child-bearing age and providing vaccination if necessary (pre-conceptual and infertility consultations).[63]
4. Screening to determine the antibody status of pregnant women with no record of vaccination or no evidence of previous immunity at first prenatal visit to determine susceptibility. Any woman with positive IgG for rubella does not require screening for rubella immunity in subsequent pregnancies. Women who have 2 documented vaccine doses or positive IgG serology do not need any serological screening thereafter, not even in subsequent pregnancies.
5. Providing programs to ensure postpartum immunization of non-immune women before they are discharged from the hospital.
6. Screening for immunity and vaccination, if necessary, of all health care personnel, including students in training.[64]
7. Immunizing all immigrant and refugee women at their first encounter with the Canadian health care system, unless they have documentation of effective vaccination or natural immunity.
8. Women who are found to be non-immune during pregnancy should be encouraged to decrease the risk of exposure to the virus by washing hands frequently, reducing close contact with individuals with viral-like illness, and avoiding travel to endemic countries. Susceptible household contacts should be vaccinated to protect the mother and fetus.[65]
9. Women with low rubella antibodies levels despite documented prior immunization with 2 doses of a rubella-containing vaccine should not be revaccinated and do not need any serological screening thereafter, as 1 lifetime dose of rubella vaccine after the age of 12 months is considered sufficient for life-long immunity (most women in Canada receive 2 doses of MMR for protection against measles and mumps, not rubella—see the section on the Rubella vaccine earlier), and, if documented with certainty, no further rubella vaccination is required following delivery even in cases where no rubella IgG is detectable by conventional assays.[56,60]

Table 3. Guidelines for the interval between administration of immune globulin preparations or blood products and MMRMMRV, or univalent varicella vaccine to maximize immunization effectiveness

Immune globulin or blood product	Dose, route	Interval between receipt of immune globulin or blood product and subsequent administration of MMR, MMRV, or univalent varicella vaccine (months)
Standard immuno globulin (human)[a]		
Immuno globulin	0.02–0.06 mL/kg, IM	3
	0.25 mL/kg, IM	5
	0.50 mL/kg, IM	6
Intravenous immuno globulin (IVIG)	300–400 mg/kg, IV	8
	1000 mg/kg, IV	10
	2000 mg/kg, IV	11
Blood transfusion products		
Plasma and platelet products	10 mL/kg, IV	7
Whole blood	10 mL/kg, IV	6
Packed red blood cells	10 mL/kg, IV	5
Reconstituted red blood cells	10 mL/kg, IV	3
Washed red blood cells[b]	10 mL/kg, IV	0
Specific immune globulin (human)		
Cytomegalovirus immune globulin (CMIVG)	150 mg/kg, IV	6
Hepatitis B immune globulin (HBIG)	0.06 mL/kg, IM	3
Rabies immune globulin (RABIG)	20 IU/kg, IM	4
Rh immune globulin (RHIG)	300 μg, IM	3[c]
Tetanus immune globulin (TIG)	250 units, IM	3
Varicella immune globulin (VARIG)	125 IU/10 kg, IM	5
Specific immune globulin (humanized monoclonal antibody)		
Respiratory syncytial virus monoclonal antibody (palivizumab) (RSVAb)	15 mg/kg/4 weeks, IM	0

IV: intravenously; IM: intramuscularly.

Adapted from the National Advisory Committee on Immunization. Blood products, human immune globulin and timing of immunization. Part 1 - key immunization information. In: Canadian Immunization Guide Ottawa: Government of Canada; 2013, Available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-11-blood-products-human-immune-globulin-timing-immunization.html#p1c10t1. Accessed on August 10, 2018. Permission to reproduce this table from the document "Key Immunization Information" has been granted by the Public Health Agency of Canada.

[a] Immune globulin can also be administered subcutaneously (SCIg). SCIg is primarily indicated as life-long replacement therapy in patients with primary antibody deficiencies for whom immunization with live vaccines is contraindicated. However, potential alternative indications for SCIg therapy may result in temporary use and discontinuation of therapy. Because pharmacokinetic properties of IgG following SCIg administration have been shown to resemble those following IVIg administration, the recommended interval between the administration of SCIg and MMR, MMRV, or univalent varicella vaccines should be considered equivalent to the recommended interval after the corresponding IVIg monthly dosing.

[b] Washed red blood cells are infrequently used.

[c] Refer to Rh immune globulin[62] for additional information.

10. In cases where immunization history cannot be confirmed and where there is no serological evidence of immunity, administration of a booster dose of MMR postpartum is not harmful and may benefit individuals who did not respond to primary immunization.

Recommendation

7. Women wishing to conceive should be counselled and encouraged to have their rubella antibody status determined if no record of rubella past immunity and no proof of immunization are available and undergo rubella vaccination if needed (III-B).

ERADICATION

There are several reasons why rubella, a vaccine-preventable disease, can be eradicated if effective vaccination programs are created around the globe. First, there are no reservoirs,

and the only organisms vital for transmission are human beings. Second, the time for contagiousness is short, and most of the time those infected become immune for life. Finally, there are accurate serological tests and effective attenuated-live vaccines available. The latter confers immunity after only 1 dose in 95% to 97% of cases and in 99% after the second dose, if the first is given at 12 months. However, since it is a highly contagious disease, vaccine coverage of up to 95% is required to interrupt rubella transmission.[8]

CONCLUSION

The mainstays of CRS prevention are the universal immunization of all Canadian infants and the identification and immunization of women at risk. Rubella infection of a pregnant woman may have devastating effects on the developing fetus. The diagnosis of infection during pregnancy should be made as soon as possible.

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