

No. 357-Immunization in Pregnancy

This Clinical Practice Guideline supersedes the original that was published in November 2009.

This clinical practice guideline has been 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: Pregnancy, immunization, vaccine, vaccination, contraindications

Outcomes: Outcomes evaluated include effectiveness of immunization and risks and benefits for mother and fetus.

Evidence: The Medline and Cochrane databases were searched for articles published up to January 2017 on the topic of immunization in pregnancy.

Values: The evidence obtained was reviewed and evaluated by the Infectious Diseases Committee of the SOGC under the leadership of the principal authors, and recommendations were made according to guidelines developed by the Canadian Task Force on Preventive Health Care (Table 1).

Benefits, Harms, and Costs: Implementation of the recommendations in this guideline should result in more appropriate immunization of pregnant and breastfeeding women, decreased risk of contraindicated immunization, and better disease prevention.

WHAT'S NEW?

1. All pregnant women should be offered a Tdap vaccine between 21-32 weeks.
2. Women with risk factors for hepatitis B, hepatitis A, meningococcal and pneumococcal disease should be vaccinated during pregnancy.
3. The prenatal care provider should play an active role in ensuring prenatal patients are educated and have access to appropriate immunizations during pregnancy.

KEY MESSAGES

1. The prenatal care provider plays a pivotal role in a pregnant patient's acceptance of a vaccine during pregnancy.
2. Many vaccines are safe for use during pregnancy.
3. The influenza vaccine is universally recommended for all pregnant women.
4. The Tdap vaccine is universally recommended for all pregnant women.

Abstract

Objective: To review the evidence and provide recommendations on immunization in pregnancy.

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Women have the right and responsibility to make informed decisions about their care in partnership with their health care providers. To facilitate informed choice, women should be provided with information and support that is evidence based, culturally appropriate, and tailored to their needs. The values, beliefs, and individual needs of each woman and her family should be sought, and the final decision about the care and treatment options chosen by the woman should be respected.

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 one 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 one 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 the 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

^aThe 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.

^bRecommendations included in these guidelines have been adapted from the Classification of recommendations criteria described in The Canadian Task Force on Preventive Health Care.

Recommendations:

- Health care providers should obtain a relevant immunization history from all women accessing prenatal care and offer vaccinations as indicated (III-A).
- In general, live and/or live-attenuated virus vaccines should not be administered during pregnancy because there is a largely theoretical risk to the fetus (II-3B).
- Women who have inadvertently received vaccination with a live or live-attenuated vaccine during pregnancy should not be counselled to terminate the pregnancy for the reason of a teratogenic risk (II-2A).
- Non-pregnant women receiving a live or live-attenuated vaccine should be counselled to delay pregnancy for at least 4 weeks (III-B).
- Inactivated viral vaccines, bacterial vaccines, and toxoids can be used safely in pregnancy (II-1A).
- Breastfeeding is not a contraindication to vaccination (passive-active immunization, live, with the exception of yellow fever, or killed vaccines) (II-1A).
- All pregnant women should be offered the diphtheria and tetanus toxoids and acellular pertussis vaccine during the second or third trimester, preferably between 21 and 32 weeks gestation, during every pregnancy, irrespective of their immunization history (II-2A).
- All pregnant women, at any stage in pregnancy, or women who might be pregnant in the upcoming influenza season, should be offered the inactivated influenza vaccine for the prevention of maternal and infant influenza-related morbidity and mortality (I-1A).
- Pregnant women with suspected or documented influenza infection, regardless of immunization history, should be treated with oseltamivir (Tamiflu, 75 mg po twice daily) (III-B).
- Some pregnant women should be offered the hepatitis B, hepatitis A, meningococcal, and/or pneumococcal vaccines for the prevention of maternal morbidity if they have specific risk factors by means of their medical comorbidities or specific exposures (III-A).

INTRODUCTION

Immunization programs are among the most cost-beneficial health interventions. Women interact with the health care system regularly during the preconception period and during pregnancy; therefore, obstetrical care providers are well-placed to review their immunization status and recommend vaccinations. This can significantly reduce the occurrence of preventable diseases, benefiting not only the woman and her infant but also the rest of the population.

The overall objective of vaccination in pregnancy is to induce a state of immunity such that the woman and the fetus are protected following exposure to the organism for which the immunization is given. In addition, this offers an opportunity for protection of the neonate for the first few months of life.

Vaccines may be prepared from various sources, including the inactivated agent, live-attenuated agent and modified and single antigen recombinant forms of the organism. Active immunization relies on the administration of antigens and results in a prompt but transient IgM response in the host. This is followed by a rise in IgG antibody production that will be more or less sustained. In cases in which the response is not sustained, booster doses may be required for long-term immune memory. Of note, oral vaccines will stimulate IgA initially as opposed to IgM (parenteral).

This document reviews indications for and contraindications to immunization during pregnancy and makes recommendations for the use of specific vaccines during pregnancy, acknowledging that immunization schedules in Canada vary according to province and territory, despite calls for harmonization^{1,2} (Table 2).

IMPORTANCE OF THE PRENATAL CARE PROVIDER AS AN IMMUNIZATION ADVOCATE

Prenatal care providers should obtain a thorough immunization history. In many cases, women present for prenatal

ABBREVIATIONS

CRS	congenital rubella syndrome
GBS	Guillain-Barré syndrome
HIV	human immunodeficiency virus
HPV	human papilloma virus
IPD	invasive pneumococcal disease
MMR	measles, mumps, rubella
RCT	randomized controlled trial
Td	tetanus toxoids and diphtheria vaccine
Tdap	tetanus toxoids, diphtheria and acellular pertussis vaccine
WHO	World Health Organization

care without having had their immunization status reviewed since they completed the school-age vaccination schedule. Digital tools like CANimmunize (digital immunization record for all Canadians to securely track, store, and update immunization records on a smartphone) can facilitate this review.

Prenatal care provides a unique window of opportunity to offer specific killed or recombinant vaccines for maternal or infant benefit and to arrange for postpartum immunization with live-attenuated vaccines as needed. Furthermore, prenatal care providers improve women’s knowledge and acceptance of vaccination.^{3,4} A recent study surveyed pregnant women to inquire about the top motivators for receiving the influenza vaccine in pregnancy, and the most important reason cited by 83% of respondents was “obstetrician recommended it.”⁵ A second survey-based study found that 83% of pregnant women considered their physician to be the most trusted source of information about vaccination in pregnancy.⁶

Recommendation

1. Health care providers should obtain a relevant immunization history from all women accessing prenatal care and offer vaccinations as indicated (III-A).

REVIEW OF SPECIFIC VACCINE CATEGORIES

Live and Live-Attenuated Vaccines

In general, live and/or live-attenuated virus vaccines are contraindicated during pregnancy because there is a theoretical risk of infection to the fetus. To date, however, there is no evidence to demonstrate a teratogenic risk from any currently available live product (e.g., MMR, varicella).^{7,8} Hence, inadvertent vaccination should not be an indication for termination of pregnancy. With the exception of the yellow fever vaccine, these products are safe and acceptable for breastfeeding mothers.

Rubella Vaccine

Rubella virus can be transmitted to the fetus and may manifest as CRS, which is particularly severe and more common if it occurs early in pregnancy, with up to 85% of infants affected if infected in the first trimester. CRS may result in deafness, cataracts, cardiac defects, microcephaly, mental retardation, hepatosplenomegaly, bone damage, and thrombocytopenia. Furthermore, the effects may be delayed by several years, and children may present with diabetes or a progressive encephalopathy. The best way to eradicate CRS is to immunize all susceptible women and women without adequate proof of immunization.

Table 2. Indications for vaccine use in pregnancy

Vaccine	Use in pregnancy	Use in breastfeeding	Comment
Live and Live-attenuated			
Influenza live-attenuated (Flumist®)	Contraindicated	Use if indicated	No known fetal adverse effects but theoretical risk to the fetus from administration of a live virus vaccine during pregnancy. Use non-live influenza vaccine formulations.
Herpes Zoster	Contraindicated	Contraindicated	Unlikely to be used among pregnant or breastfeeding patients given age indications for use
Measles-Mumps-rubella	Generally Contraindicated	Recommended if not Immune	No known fetal adverse effects but theoretical risk to the fetus from administration of a live virus vaccine during pregnancy.
Poliomyelitis (oral polio vaccine: OPV)	Contraindicated; not available in Canada		No known fetal adverse effects but theoretical risk to the fetus from administration of a live virus vaccine during pregnancy. Consider using the inactivated polio vaccine (see "Poliomyelitis: IPV" below).
Oral Typhoid	Contraindicated	Not recommended	No known fetal adverse effects but theoretical risk to the fetus from administration of a live virus vaccine during pregnancy. Use parenteral typhoid if indicated –see below under non-live-.
Vaccinia	Contraindicated	Generally contraindicated unless high-risk situation	Not known to cause congenital malformations, but can cause fetal infection and adverse pregnancy outcomes
Varicella	Contraindicated during pregnancy. Indicated postpartum if susceptible (see text).	Recommended if not immune	Fetal effects, if any, unknown.
Yellow Fever	Generally contraindicated, unless high-risk situation	Generally contraindicated	No data on fetal safety, although fetuses exposed have not demonstrated complications. Not a reason for pregnancy termination. If travel to high-risk endemic area unavoidable, suggest vaccination. If Yellow Fever vaccine is required for entry into a country, but the country is not recognized as an endemic area, pregnancy is grounds for exemption from vaccination. Cases of infant meningoencephalitis associated with vaccination of breastfeeding mothers have been reported
Non-Live			
Cholera	Consider in high-risk situations only	Use if indicated	No data on safety.
Haemophilus influenza B	Indicated for certain maternal conditions	Use if indicated	No data on safety.
Hepatitis A	Indicated in pregnancy in certain circumstances	Use if indicated	No apparent fetal risk.
Hepatitis B	Indicated in pregnancy in certain circumstances	Use if indicated	Indicated if pregnant woman is at risk of hepatitis B acquisition during pregnancy and is susceptible to infection
Human papillomavirus	Not recommended Limited data on use in pregnancy	Use if indicated	No intervention required if vaccine administered during pregnancy. Delay HPV series until postpartum period. The series do not need to be restarted if interrupted.
Influenza	Universally recommended in pregnancy	Recommended if not immunized during pregnancy	Trivalent and quadrivalent influenza vaccines protect mother, fetus and infants from influenza-related morbidity and mortality.

Continued

Table 2. Continued

Vaccine	Use in pregnancy	Use in breastfeeding	Comment
Inactivated Japanese encephalitis vaccine	Consider only if travel where risk exposure is high (benefit>risk).	Use if indicated in high risk situations	No data on use in pregnancy Not to be given routinely in pregnancy, as theoretical risk exists.
Meningococcal Conjugated	Indicated in high-risk situations or medical conditions	Indicated in high-risk situations or medical conditions	No data on use in pregnancy Use if indicated as per adult guidelines (travel to a high-risk area, post-exposure prophylaxis or outbreak situation).
Plague	Consider if benefits outweigh risk.	Indicated in high-risk situations	No data on safety in pregnancy
Pneumococcal Conjugated	Indicated in high-risk patients	Use if indicated	No safety data available, but no adverse effects reported. Indicated in women at high risk of invasive pneumococcal disease.
Pneumococcal Polysaccharide	Indicated in high-risk patients	Use if indicated	Indicated in women at high risk of invasive pneumococcal disease.
Poliomyelitis (inactivated polio vaccine: IPV)	Indicated in high-risk situations	Use if indicated	Pregnancy is a not contraindication for post-exposure prophylaxis.
Rabies	Indicated if potential exposure to rabies	Use if indicated	No evidence of fetal adverse outcomes Pregnancy not a contraindication to post-exposure prophylaxis.
Tdap (diphtheria and tetanus toxoids and acellular pertussis)	Indicated in every pregnancy	Recommended if no dose received in adulthood	Td and TdaP considered safe in pregnancy. Benefit to infant from maternal vaccination in the second or third trimester of pregnancy.
Typhoid Parenteral	Consider only in high-risk cases (e.g., travel to endemic areas).	Use if indicated	No data on safety in pregnancy

The rubella vaccine alone and in combination is a live vaccine and therefore is generally contraindicated during pregnancy, but may be considered during outbreaks of rubella and measles, where the benefit outweighs the risks. Inadvertent vaccination in pregnancy was reportable to the Centers for Disease Control and Prevention between 1971 and 1989. Analysis of the accumulated data revealed that subclinical infection was detected in 1% to 2% of fetuses but that there was no evidence of CRS in any of the 321 women inadvertently vaccinated who elected to continue their pregnancies.⁹ Therefore, in such situations, women should be reassured that ending the pregnancy is not necessary on the basis of fetal risks following maternal immunization. However, given the small theoretical fetal risk, immunization with the rubella vaccine is best delayed until after delivery.

Immunity to rubella can be assumed if there is documentation of an individual having received 1 dose of a rubella vaccine (e.g., MMR) after 12 months of age, laboratory-confirmed disease, or laboratory evidence of immunity.¹⁰ Some individuals do not mount an immune response that produces high levels of rubella IgG as detected by routine assays. However, immune studies of these individuals following a booster dose of the rubella vaccine demonstrate an immune

response consistent with prior immunity.^{11,12} One life-time dose of rubella vaccine after the age of 12 months is considered sufficient for life-long immunity and, if documented with certainty, no additional rubella vaccination is required following delivery, even in cases for which no rubella IgG is detectable by conventional assays.¹⁰ In cases in which prior immunization history cannot be confirmed and there is no serologic 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.

In addition, it is recommended to delay conception for 4 weeks after receiving a rubella vaccine. Neither breastfeeding nor Rh-immunoglobulin is a contraindication to immunization against rubella. However, it is advisable to consider delaying vaccination if the patient received Rh-immune globulin or other blood products.¹³ The obstetrical care provider is in a good position to identify susceptible women and to provide immunization postpartum.

Varicella Vaccine

Although varicella is relatively uncommon in the pregnant population (0.7 per 1000), it can result in very significant maternal, fetal, and infant morbidity and mortality. Despite improvements in clinical care, varicella may be compli-

cated by pneumonia in up to 28% of pregnant women, and this remains associated with a risk of maternal mortality.¹⁴ Furthermore, varicella in early pregnancy is associated with a 1% risk of congenital infection, which carries serious sequelae such as cerebral cortical atrophy, mental retardation, and dermatomal-specific limb abnormalities.¹⁵ Maternal varicella occurring 5 days before to 2 days after delivery is associated with severe neonatal varicella in 17% to 30% of infants and a case fatality rate as high as 31%.¹⁶

Immunity to varicella should be reviewed, ideally prior to pregnancy, for all women in the priority groups for varicella vaccination including people who work with young children, health care workers, and people who emigrated from tropical regions. Because the varicella vaccine is a live-attenuated virus vaccine (2 preparations are available in Canada and both are live), it should not be given in pregnancy but rather preconceptionally or in the postpartum period, per national guidelines.¹⁷

Breastfeeding is not a contraindication to vaccination with varicella vaccine nor is household contact with a newborn. A study of 362 women inadvertently exposed to varicella vaccine in pregnancy between 1995 and 2000 identified no cases of congenital varicella.¹⁸ Therefore, inadvertent vaccination with varicella vaccine during pregnancy does not constitute a reason to recommend pregnancy termination.

Benefits Versus Risks of Live-Attenuated Vaccines during Pregnancy

Given the possible risks, live-attenuated vaccines should not be given in pregnancy unless there are special circumstances and the benefits clearly outweigh the theoretical risks. For example, if a pregnant woman must travel to an area at high risk of yellow fever transmission, travel cannot be postponed, and high level of mosquito protection is not feasible, the vaccine may be administered, even though it is a live-attenuated vaccine. A recent report of 304 pregnant women exposed to yellow fever immunization in early pregnancy demonstrated that such exposure was not associated with an increase in major fetal malformation.¹⁹ Many countries require yellow fever vaccination prior to entry, but risk of yellow fever transmission is not an issue in all of them (refer to http://www.who.int/ith/ITH_Annex_I.pdf). In cases for which vaccination against yellow fever is an entry requirement into a country, but where yellow fever is not endemic, pregnancy constitutes medical grounds for exemption from the vaccination requirement. It may be beneficial for a pregnant woman to seek advice about travel vaccinations from a travel clinic staffed with providers who have experience counselling pregnant women.

Recommendations

2. In general, live and/or live-attenuated virus vaccines should not be administered during pregnancy because there is a largely theoretical risk to the fetus (II-3B).
3. Women who have inadvertently received vaccination with a live or live-attenuated vaccine during pregnancy should not be counselled to terminate the pregnancy for the reason of a teratogenic risk (II-2A).
4. Non-pregnant women receiving a live or live-attenuated vaccine should be counselled to delay pregnancy for at least 4 weeks (III-B).

Inactivated Viral Vaccines, Bacterial Vaccines, and Toxoids

These vaccines are considered safe in pregnancy. Because there is no evidence to suggest a risk to the fetus or to the pregnancy from maternal immunization with these agents, the benefit of their use generally far outweighs the theoretical risks.

Recommendations

5. Inactivated viral vaccines, bacterial vaccines, and toxoids can be used safely in pregnancy (II-1A).
6. Breastfeeding is not a contraindication to vaccination (passive-active immunization, live, with the exception of yellow fever, or killed vaccines) (II-1A).

Tdap Vaccine

There has been a long experience with the safe administration of tetanus toxoid (with or without diphtheria toxoids) during pregnancy; indeed, in the developing world, the use of these vaccines has led to the virtual eradication of neonatal tetanus. Adult formulations of the acellular pertussis vaccine (Tdap; Adacel [Sanofi Pasteur, Lyon, France] and Boostrix [GlaxoSmithKline, Rixensart, Belgium]) are available in Canada and are recommended for universal immunization of adolescents. A single adult dose of Tdap is also recommended for all adults to replace their next 10 annual dose of Td.

The burden of severe disease from infection with *Bordetella pertussis* falls largely on very young infants, under 2 months of age, who are too young to be vaccinated. Between 2010 and 2014, an increase in the incidence of pertussis among infants was noted in certain jurisdictions in Canada, the United States, and Great Britain, prompting the evaluation of a strategy for maternal immunization against pertussis.^{20,21}

Transplacental passage of pertussis antibodies is clearly demonstrated.^{22,23} Transplacental passage of immunoglobulins is minimal until 13 to 16 weeks' gestation, followed by a continuous increase in the second trimester and a sharp increase in the third trimester. The reason for this increase is not entirely clear but is theorized to be secondary to the increased expression of the Fc receptor on syncytiotrophoblastic tissue throughout gestation. There are conflicting data about the optimal timing of maternal vaccination to allow for the highest concentrations of pertussis antibodies in infants, and the role of immunoglobulin avidity requires additional study.^{24–33}

A number of prospective trials have demonstrated that high antibody levels conferred to infants by transplacental passage after maternal vaccination are associated with lower antibody levels to certain pertussis antigens subsequent to their own childhood vaccination series.^{23,34–36} This phenomenon is referred to as immuneblunting. The precise antigens affected by immuneblunting and the degree of effect varies among these studies.^{23,34–36} It is important to consider that we have no serological correlate for immunity against pertussis. As such, the clinical significance of lower antibody levels remains to be determined. Additional data are being acquired to delineate the effect of immune blunting on the immunogenicity of an infant's primary vaccine series.³⁷

Population-based evidence from countries with universal maternal pertussis immunization programs demonstrating efficacy of maternal Tdap vaccination to prevent infant pertussis continues to grow. Specifically, four retrospective observational studies and one case-control study demonstrated clinical efficacy of maternal vaccination with Tdap for the prevention of infant morbidity and mortality.^{38–42} Two British studies compared rates of maternal vaccination among infants who developed pertussis aged <3 months with rates of maternal vaccination among control patients, and both studies estimated effectiveness of maternal Tdap vaccination to be approximately 91% for the prevention of clinically proven pertussis in infants <3 months.^{41,42} A retrospective US study from the Kaiser-Permanente medical organization compared 74 504 women who had received Tdap either during the antepartum or postpartum period and found that antepartum administration between 27 and 36 weeks GA was superior to postpartum administration and demonstrated an 85% vaccine effectiveness for the prevention of pertussis in infants aged <8 weeks.³⁸ Most recently, a retrospective study of 148 981 newborns from California demonstrated that maternal immunization with Tdap at least 8 days before birth is associated with an 88% vaccine efficacy for the

first 2 months of infancy. Moreover, this group demonstrated continued evidence for vaccine efficacy of maternal vaccination following an infant's primary diphtheria, tetanus and acellular pertussis series and up to 12 months of life.³⁹

A Canadian multi-site RCT of 273 pregnant women demonstrated no difference in adverse maternal or obstetrical adverse events following administration of Tdap compared with Td.³⁷ The use of Tdap in pregnancy appears to be safe,^{43–45} even if less than 2 years have elapsed since the time of the last tetanus vaccine.⁴⁶ The WHO has promoted maternal vaccination with Tdap as the most cost-effective strategy for preventing pertussis in infants too young to be vaccinated.⁴⁷

In brief, all pregnant women should be offered the Tdap vaccine, regardless of current and local pertussis epidemiology, because pertussis outbreaks are sporadic and difficult to predict, and there could be lag time in detection of an outbreak and subsequent reactive immunization. Tdap can be offered at any prenatal appointment; after 13 weeks based on available data; however, immunization between 27 and 32 weeks of gestation maximizes passive antibody transfer to the infant. One must keep in mind that a systematic delay of vaccination may lead to missed opportunities among women who deliver preterm, so immunization as early as 21 weeks (usually after the routine anatomical ultrasound) is encouraged. Maternal vaccination after 32 weeks or in the postpartum period still confers some protection to the infant and should be recommended if a dose of Tdap has not yet been provided during the pregnancy.

Recommendation

- All pregnant women should be offered the diphtheria and tetanus toxoids and acellular pertussis vaccine during the second or third trimester, preferably between 21 and 32 weeks gestation, during every pregnancy, irrespective of their immunization history (II-2A).

Influenza Vaccine

There is literature demonstrating that pregnant women are at increased risk of influenza-related hospitalization and serious complications, including mortality.^{48,49} Pregnancy is associated with significant cardiovascular and respiratory demands, as evidenced by increases in stroke volume, heart rate, and oxygen consumption. More recent studies have shown an increase in influenza-related hospitalization of healthy pregnant women, with seasonal influenza occurring at the rate of 1 per 1000, or 0.1%.^{50–55}

The risks were in fact calculated to be equivalent to those of non-pregnant women with high-risk conditions, for whom immunization has traditionally been recommended. Older data^{56,57} also suggest increased maternal risk; previous reports of pandemics showed that morbidity and mortality were greater in pregnant women.

Neither influenza nor influenza vaccine is teratogenic.⁵⁸ Large studies have not found such an association between influenza immunizations and pregnancy loss or other adverse pregnancy outcomes.^{59–61} A small case-control study reported that among women receiving H1N1-containing influenza immunizations over 2 consecutive years, there was an association between receipt of the seasonal influenza vaccination and spontaneous abortion within 28 days of immunization.⁶² This association has not been seen in other larger studies. Passive surveillance has not revealed any safety concerns about using inactivated influenza vaccine in pregnancy over decades,^{63,64} and surveillance following the use of pandemic influenza A (H1N1) vaccines in more than 100 000 pregnant women in Canada and more than 488 000 pregnant women in Europe also did not reveal any safety concerns.^{65,66}

Another reason for immunization in pregnancy is the protection of the fetus and newborn after birth, which can be accomplished with passive immunity (transfer of maternal antibodies). RCT evidence demonstrates that the administration of the influenza vaccine during pregnancy reduces febrile influenza-like illness in pregnant women by over 30% and also reduces proven influenza infections in 0- to 6-month-old infants by 63%. The same group reported that at times in which influenza was circulating in the environment, infants born to women who had received the influenza vaccine were less likely to be born SGA.⁶⁷ In addition, retrospective data also demonstrate a reduction in the rate of stillbirth among mothers who have received the influenza vaccine during pregnancy.⁶⁸

Current Canadian recommendations advocate universal immunization of pregnant women in any trimester against influenza⁵⁷ and influenza immunization of the caregivers and family of young infants.⁶⁹

H1N1 in Pregnancy

In 2009, H1N1 of swine origin emerged as a pandemic strain and resulted in increased morbidity and mortality among pregnant and postpartum women, including up to 4 weeks after delivery.^{57,70} Hospitalization rates were as high as 32%.⁷¹ A significant increase in stillbirths, premature deliveries, and infant mortality was documented among maternal H1N1 infections in the third trimester.⁷²

Antiviral Treatment

Oseltamivir in standard doses is recommended for treatment of pregnant women with influenza, (including seasonal influenza) given the higher risk for influenza complications in this population.⁷³ The safety of oseltamivir in pregnancy and lactation has been reviewed, and its extensive use during the H1N1 pandemic confirmed its safety and acceptability in pregnancy.⁷⁴ Zanamivir may also be used, although the safety data are much more limited. In addition, both drugs can be used safely during breastfeeding.

Recommendations

8. All pregnant women, at any stage in pregnancy, or women who might be pregnant in the upcoming influenza season, should be offered the inactivated influenza vaccine for the prevention of maternal and infant influenza-related morbidity and mortality (I-1A).
9. Pregnant women with suspected or documented influenza infection, regardless of immunization history, should be treated with oseltamivir (Tamiflu, 75 mg po twice daily) (III-B).

OTHER VACCINES

Hepatitis B Vaccine

Acute maternal hepatitis B infection during pregnancy poses a high risk of mother-to-child transmission (up to 60% in the third trimester). These infants have a 70% to 90% risk of chronic hepatitis B infection. Pregnant women at high risk for acquiring hepatitis B infection during pregnancy (e.g., more than 1 sex partner during the previous 6 months, been evaluated or treated for a sexually transmitted disease, recent or current injection drug use, having had a hepatitis B-infected sex partner, health care workers and household contacts of hepatitis B-infected individuals) and who are susceptible to hepatitis B infection (hepatitis B surface antigen and antibody negative) should be offered recombinant hepatitis B vaccine series. Pregnancy is not a contraindication for immunization to hepatitis B virus. Immunization of susceptible pregnant women is highly immunogenic (84%–100%) and effective to confer anti-HBs to the newborn (60%–100%).^{75,76} Limited data suggest that developing fetuses are not at risk for adverse events when hepatitis B vaccine is administered to pregnant women.

Human Papilloma Virus Vaccine

In Canada, the bivalent, quadrivalent, and nonavalent HPV vaccines are now available for the prevention of infection by HPV strains that are responsible for the vast majority of cases of cervical cancers and genital warts. The available HPV vaccines are manufactured using recombinant

Table 3. Medical conditions resulting in high risk of IPD⁷⁸

Risk group	Underlying medical condition
Immunocompetent persons	Chronic heart disease Chronic lung disease Diabetes mellitus Cerebrospinal fluid leak Cochlear implant Alcoholism Chronic liver disease, cirrhosis Cigarette smoking
Persons with functional or anatomical asplenia	Sickle cell disease/other hemoglobinopathy Congenital or acquired asplenia
Immunocompromised persons	Congenital or acquired immunodeficiency HIV infection Chronic renal failure Nephrotic syndrome Leukemia Lymphoma Hodgkin disease Generalized malignancy Iatrogenic immunosuppression Solid organ transplant Multiple myeloma

technology and use a specific subunit of the virus L1, which then assembles into non-infectious virus-like particles. Although the vaccine is not recommended for use during pregnancy, there is no evidence that it is teratogenic.⁷⁷ If a woman becomes pregnant part way through the vaccine series, the rest of the series should be deferred until after pregnancy. The vaccine series does not need to be restarted postpartum.⁷⁸ The vaccine can be administered to women who are breastfeeding.⁷⁷

Hepatitis A Vaccine

Hepatitis A follows a severe course in pregnancy, including reported cases of liver failure. The vaccine should be considered for pregnant women travelling to an endemic area for post-exposure prophylaxis (close contact with a person with hepatitis A infection).

Pneumococcal Vaccines

Pregnancy per se does not seem to be a risk factor for IPD, but pneumococcus is still the most common cause of bacterial meningitis in pregnancy. Some pregnant women are at higher risk of IPD, mostly on the basis of their medical comorbidities (Table 3). Pregnant women at risk of IPD who have not been immunized prior to pregnancy against pneumococcus should be counselled to start the pneumococcal immunization series.

Recommendation

10. Some pregnant women should be offered the hepatitis B, hepatitis A, meningococcal, and/or pneumococcal vaccines for the prevention of maternal morbidity if they have specific risk factors by means of their medical comorbidities or specific exposures (III-A).

SIDE EFFECTS OF VACCINES AND CONTRAINDICATIONS

Vaccines may cause various side effects, which should not all be interpreted as contraindications. Side effects can be divided in the following 5 categories: (1) immediate/early, (2) local, (3) systemic, (4) allergic, and (5) long term.

1. Immediate/early effects include fainting and vasovagal reactions. These are differentiated from anaphylactic shock (see in the following list). Patients who have received a vaccine should be kept in the waiting room for observation for 15 to 30 minutes.
2. Local effects are mild and are the most common. They include soreness, erythema, and swelling.
3. Systemic effects are less common and include malaise and fever.
4. Mild allergic reactions can also occur. In general, these will be in reaction to exposure to avian proteins (eggs, such as in yellow fever vaccine and influenza vaccine) or to traces of neomycin/streptomycin (MMR). Anaphylactic reactions are exceedingly rare and should be recognized immediately and treated following local protocols with injection of subcutaneous epinephrine (1:1000).
5. GBS can be temporally associated with vaccination. This risk has been estimated as very small (1 excess case of GBS per 1 million people vaccinated) and certainly much lower than the risk of spontaneous GBS occurrence, usually seen in association with naturally occurring viral or bacterial infections, such as influenza (2 cases per 100 000 person/years).^{79,80}

Vaccines are contraindicated in situations in which the risk of adverse reactions based on history or current clinical condition outweighs any potential therapeutic benefits. General contraindications include the following:

- Anaphylaxis to a vaccine or a vaccine component
- Severe uncontrolled asthma
- History of GBS within 6 months of receiving a vaccine (contraindicated if receiving the same vaccine)

Vaccination of immunocompromised individuals must include the consideration of the type and degree of immunosuppression and the fact that the degree of immunosuppression may vary over time. In general, severely immunocompromised individuals should not receive live vaccines. Modified vaccine schedules are still recommended for HIV-positive individuals, solid organ and hematopoietic stem cell transplantation recipients, and those undergoing immunosuppressive therapies. For a comprehensive list of contraindications, according to specific vaccine products, and immunization of immunocompromised individuals, refer to the Canadian Immunization Guide.⁷⁸

The items on this list do not represent contraindications to immunization:

- Mild acute illness with or without low-grade fever
- Autoimmune disorder, multiple sclerosis
- Family history of convulsions, epilepsy
- Recent exposure to an infectious disease
- Current antimicrobial therapy or convalescence from recent illness
- Household contact with pregnant woman
- Breastfeeding
- Prior reaction to immunization with mild/moderate tenderness, redness, swelling, or fever under 40°C
- Personal history of allergies, excluding anaphylaxis, to neomycin/streptomycin or egg protein
- Family history of adverse reaction or allergies to vaccines
- Positive tuberculosis skin test

Two of these circumstances deserve additional discussion: household contact vaccination and breastfeeding. Although individuals immunized with some live virus vaccines can shed the virus, they usually do not transmit it; therefore, household contacts of pregnant women can be safely vaccinated without risks to the mother and her fetus. Breastfeeding is also considered safe following immunization of the mother, and it has not been shown to adversely influence the maternal immune response. Therefore, breastfeeding does not represent a contraindication to any immunization—passive-active immunization, live vaccines, or killed vaccines.

CONCLUSION

The development of new vaccines and the accumulating information about vaccine safety ensure that health care providers can provide immunizations and/or advice about immunization for their pregnant patients. This is most important in disease prevention, and antenatal care providers

must play an active role in vaccine counselling and administration. Furthermore, it is imperative that more research efforts be focused in the area of immunization in pregnancy.

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