Alberta COVID-19 Immunization in Pregnancy Factsheet for Practitioners - update

*This summary is based on information available up to May 28, 2021. Contents are subject to change as new information becomes available.

SOGC Statement on COVID-19 Vaccination in Pregnancy (Updated May 25, 2021) and SOGC Statement on the COVID-19 Vaccines and Rare Adverse Outcomes of Thrombosis Associated with Low Platelets (Updated April 20, 2021)

CONSENSUS STATEMENTS:
1. Pregnant individuals should be offered immunization at any time during pregnancy or while breastfeeding if no contraindications exist.
2. The SOGC supports the use of all available COVID-19 vaccines approved in Canada in any trimester of pregnancy and during breastfeeding in accordance with provincial and territorial guidelines on type of vaccine to prioritize for pregnant and breastfeeding individuals. *
3. The decision to be immunized is based on the individual’s personal values, as well as an understanding that the risk of infection and/or morbidity from COVID-19 outweighs the theorized and undescribed risk of being immunized during pregnancy or while breastfeeding. Individuals should not be precluded from immunization based on pregnancy status or breastfeeding.
4. Given that pregnant people are at increased risk of morbidity from COVID-19 infection, all pregnant persons should be eligible to receive a COVID-19 vaccination.

* Current Alberta Provincial and National Advisory Committee on Immunization (NACI) guidelines recommend the mRNA vaccine preferentially for pregnant individuals due to reassuring published safety data from post-marketing surveillance including 4,000 pregnant individuals vaccinated with mRNA vaccines.

Key Messages

- Pregnant patients with COVID-19 infection are at a higher risk of hospitalization, admission to the ICU, and preterm birth than non-pregnant patients of the same age.1-4
- The risk of severe morbidity from COVID-19 in pregnant women appears to be associated with risk factors including age >35 year old, asthma, obesity, pre-existing diabetes, pre-existing hypertension and heart disease.2,3
- International registry and surveillance data have not detected adverse pregnancy outcomes related to any COVID-19 vaccinations with Pfizer or Moderna vaccines.5
Emerging evidence suggests passive antibody transfer to the fetus in utero and to the infant through breastmilk.\cite{6,7}

- Individuals who may be pregnant, are pregnant or are breastfeeding have the right to receive the vaccine, should they choose to do so.\cite{8}
- Individual counselling with a clinician regarding immunization in pregnancy is recommended. However, this is not a requirement before immunization.
- Immunization is recommended regardless of prior symptomatic or asymptomatic COVID-19 infection because:
  - Prior COVID-19 infection does NOT protect from recurrent COVID-19 infection in pregnancy
  - Protective Antibodies from COVID-19 immunization are present in higher concentrations in breast milk and cord-blood compared to antibodies arising from natural infection\cite{6}
- Immunization can be scheduled once patients have recovered from their illness and completed their isolation.
- Immunization within 30-days of conception with mRNA vaccines is safe\cite{5,9}
- In the absence of evidence, it is prudent to wait\cite{9}
  - for a period of at least 28 days between the administration of a dose of COVID-19 vaccine and the administration of another vaccine (except in the case where another vaccine is required for post-exposure prophylaxis)
  - for a period of at least 14 days after the administration of another vaccine before administering a COVID-19 vaccine.

Scientific Data – COVID-19 Vaccines

There are currently four COVID-19 vaccines licensed for use in Canada: Pfizer-BioNTech COVID-19 vaccine (mRNA vaccine), Moderna COVID-19 vaccine (mRNA vaccine), AstraZeneca COVID-19 vaccine (non-replicating viral vector vaccine) and Janssen (non-replicating viral vector vaccine).

mRNA Vaccine Platforms

This model consists of messenger RNA (mRNA) encapsulated by a lipid nanoparticle (LNP), which allows the mRNA entrance into host (human) cells. The mRNA in the vaccine codes for the SARS-CoV-2 spike protein utilized by the virus to bind to human receptors and promote viral replication. The vaccine provides the host cell instructions to manufacture only this spike protein and express it on its surface. Recognizing the spike protein as a foreign antigen, the host immune system is then activated to produce an immune response.\cite{9} The mRNA does not enter the nucleus or alter human DNA and human cells do not have the machinery to allow it to do so.

The efficacy of the Pfizer-BioNTech COVID-19 vaccine has been demonstrated for adults 12 years and older in Phase II and Phase III trials involving the randomization of approximately 44,000 individuals.\cite{6} These trials demonstrated a vaccine efficacy of 94.6% for preventing symptomatic COVID-19 cases at least 7 days following the second dose.\cite{10} In Phase III trials for the Moderna COVID-19 vaccine involving the randomization of 30,000 individuals, the vaccine was reported to have 94.1% efficacy against
symptomatic COVID-19, with no serious safety concerns identified during the initial 2 month follow-up period.\textsuperscript{11}

Pregnant and breastfeeding women were excluded from the available Phase II and Phase III studies for the PfizerBioNTech and Moderna COVID-19 vaccines. Real-life data (post-marketing surveillance) from the US reporting on nearly 4,000 pregnant women who received either the Pfizer-BioNTech vaccine or the Moderna vaccine reported no differences in the rates of adverse pregnancy and neonatal outcomes for those women who were pregnant and compared to pre-pandemic rates.\textsuperscript{5} Data from the 36 reported pregnancies that happened during the Phase II and Phase III studies was reassuring as well.\textsuperscript{4}

**Non-replicating Viral Vector Vaccines**

The Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine utilizes a Chimpanzee adenovirus non-replicating vector vaccine platform. The chimpanzee adenovirus does not cause disease in humans but is used to carry part of the pathogen’s DNA into human cells where it causes the human cells to make viral proteins (in this case the spike protein of SARS-CoV-2). The viral DNA does not alter human DNA. The AstraZeneca COVID-19 vaccine was initially evaluated as a series of two intramuscular injections given 4-12 weeks apart; however, similar to the mRNA vaccines, considerable data on different dosing intervals has accrued. Preliminary Phase III data from 11,636 participants demonstrates an overall vaccine efficacy of 70.4% against symptomatic COVID-19 disease.\textsuperscript{12} Pregnant and breastfeeding women were excluded from the Phase III AstraZeneca Trials; however, 21 inadvertent pregnancies (12 in the vaccine arm and 9 in the placebo arm) were reported without adverse effects to date. Preclinical trials did not demonstrate adverse effects on fertility, pregnancy, fetal or postnatal outcomes.

International reports have documented extremely rare events of arterial and venous thrombosis in combination with low platelets following adenovirus vector COVID-19 vaccines (AstraZeneca, COVISHIELD, Janssen COVID-19 vaccines).\textsuperscript{9,13,14} These events occurred in women ages 18 – 59, with symptom onset 6 – 15 days after immunization.\textsuperscript{13} However, this may reflect a workforce gender bias due to the decision to prioritize front-line health care workers, most of whom identify as female. Furthermore, it is important to remember these specific adverse events are very rare: 1 in 55,000 doses and especially when considering Canadian data that suggests 1 in 100 hospitalized pregnant patients will require ICU admission following infection with COVID-19.\textsuperscript{1,3}

There is no known association between this syndrome and pregnancy and no physiologic basis to increase this risk in pregnancy. To date, no cases of thrombosis with thrombocytopenia in pregnant individuals have been reported.

The current Provincial and NACI guidelines recommend that mRNA vaccines are preferable for pregnant individuals. However, this recommendation may change based on several factors including vaccine availability and outcome data.
Considerations for COVID-19 Immunization During Pregnancy and Breastfeeding

Decades of experience with other vaccines administered during pregnancy would suggest that we could expect a similar efficacy for the COVID-19 vaccines in pregnant women compared to non-pregnant women. Vaccines in general are immunogenic, safe, and efficacious when delivered to pregnant women. While there have been no red flags or hypothesized mechanisms for potential harm associated with the administration of an mRNA vaccine during pregnancy, until more data is available, the potential risks of immunization to a pregnant woman and her fetus remain unknown and only theoretical. What is known, however, is that a non-immunized pregnant woman remains at risk of COVID-19 infection and remains at heightened risk of severe morbidity if infected compared to non-pregnant counterparts. Severe infection with COVID-19 carries risks to both maternal, fetal and neonatal health. Owing to maternal age or underlying comorbidities, some pregnant women are at high risk of severe COVID-related morbidity.

NACI has advised “that a complete vaccine series with an mRNA COVID-19 vaccine should be offered to individuals in the authorized age group who are pregnant. If an mRNA vaccine is contraindicated, another authorized COVID-19 vaccine should be offered. Informed consent should include discussion about emerging evidence on the safety of mRNA COVID-19 vaccines in this population. (Strong NACI Recommendation)”. 9

It is recommended that pregnant and breastfeeding women make an informed decision by having access to up-to-date information about the safety and efficacy of the vaccine, theoretical risk of harm, and potential benefits to the fetus. During an epidemic, the default should be to offer vaccines to pregnant women alongside other affected populations.4,15,16 Pregnant and breastfeeding women will likely look to their prenatal care provider to assist in making decisions weighing the risks and benefits so that they might arrive at a well informed and autonomous decision that is right for them as an individual.

Such a discussion should prioritize patient autonomy and should include, but not be limited to assessment of:

- Local epidemiology and risk of community acquisition of COVID-19
- Workplace situation and risk of work-related acquisition of COVID-19
- Individual risk for COVID-related morbidity including consideration for comorbidities such as advanced maternal age, immunosuppressive conditions, pre-existing diabetes, pre-existing hypertension, obesity or chronic respiratory/cardiac conditions
- Available data related to the safety of the vaccine during pregnancy and lactation
- Individual beliefs and personal risk assessment of the available data

Individuals who proceed with immunization

Individuals should be informed of the expected side effects following immunization. While pain at the injection site, fatigue and headache are the most commonly reported symptoms following
immunization, fever was reported 16% of the time for younger, non-pregnant individuals. Pregnant women can be counselled to treat mild post vaccination fevers with antipyretics (e.g., acetaminophen).

**Timing of immunization during pregnancy and vaccine interval**

Immunization of a pregnant woman can confer benefit to a newborn infant through a mechanism of maternal immunization similar to what is seen for pertussis and influenza immunization during pregnancy. Emerging data shows maternal antibodies to SARS-CoV-2 cross the placenta after infection or immunization. This preliminary data also suggests vaccine-generated antibody titers are higher compared to those seen following COVID-19 infection in pregnancy. Antibodies were found in umbilical cord blood and breastmilk, suggesting it is possible for maternal antibodies to transfer through the placenta and confer protection against COVID-19 infection to the fetus in utero and the neonate during lactation.

All pregnant individuals are encouraged to consider COVID-19 immunization in pregnancy, even if the patient has had a symptomatic or asymptomatic COVID-19 infection. Immunization can be given after the patient has recovered from acute illness and has completed the mandatory isolation. Ideally, a 28-day interval between receiving the COVID-19 immunization and other vaccines is recommended and 14-day interval before receiving the COVID-19 vaccine if other vaccine (e.g., Pertussis or influenza) was given first. However, practitioners can consider shorter interval administration of vaccines for high-risk individuals. The spacing recommendation is due to the theoretical risk of an increased inflammatory response, and the confusion of vaccine adverse events between different vaccines and not from data which shows a direct effect on efficacy of adverse events. In addition, administration of immunoglobulins is thought to interfere with vaccine efficacy due to circulating levels of antibody to live attenuated vaccines within the population. However, the rates of circulating antibodies to COVID-19 are low therefore the impact on vaccine efficacy of COVID-19 is unclear.

Rhogam and Betamethasone should be given as indicated for obstetrical reasons. Vaccination (COVID-19, pertussis, or flu vaccines) can be administered simultaneously or at any time before or after these treatments.

If contemplating pregnancy, ideally individuals will complete a full course of COVID-19 vaccination (2 doses) prior to becoming pregnant to gain the most benefit from vaccination throughout the whole pregnancy.

As per most recent NACI guidance, those who are trying to become pregnant do not need to avoid pregnancy after immunization with an mRNA vaccine, because US safety data suggests mRNA vaccine administration within 30 of vaccine administration is safe. Consequently, inadvertent pregnancy between doses or shortly after receiving the COVID-19 vaccine is not an indication for pregnancy termination.
References