Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COVID-19 Vaccination in Pregnancy: The Benefits Outweigh the Risks

The rapid development of a vaccine to protect against SARS-CoV-2 infection and prevent coronavirus disease 2019 (COVID-19) has been a historic scientific achievement but has also raised many questions in the health care community about vaccine safety for patients who were not included in clinical trials. As mass immunization efforts have rapidly expanded, obstetricians across the globe now face the challenge of advising pregnant patients on whether they should receive the vaccine.

The goal of any preventative prenatal intervention is to minimize risk to the fetus and mother, while maximizing health benefits. Within this context, there is precedent for immunization during pregnancy: Tetanus, diphtheria, and pertussis and influenza vaccines are routinely administered in the second or third trimester.[1] Protecting the mother against infection is a primary benefit; pregnancy functionally immunosuppresses a patient and places added stress on cardiopulmonary systems. Secondary benefits to the fetus include prevention of complications during delivery and the transmission of protective antibodies transplacentally and through breastfeeding.

Past pandemics with accelerated vaccine development timelines have included pregnant patients in immunization efforts, such as with H1N1 (swine flu). However, studies investigating vaccine uptake in the 2009 pandemic showed that few pregnant patients decided to be vaccinated against H1N1.[2,3] The highest vaccine acceptance rates were in those whose obstetricians specifically recommended immunization.[2,3] Thus, the physician plays a key role in advocating for vaccination in high-risk populations rather than perpetuating hesitancy out of fear of the unknown.

Although some live vaccinations, such as measles, mumps, and rubella and varicella, are contraindicated in pregnancy, all current COVID-19 vaccines are composed of double-stranded DNA or mRNA and do not carry the live virus (Table).[4,5] Clinical trials demonstrate that vaccination is highly effective in preventing symptomatic COVID-19 in non-pregnant patients.[4] The potential harms to pregnant patients who experience peripartum infection include increased risk of intensive care unit admission and maternal mortality.[6] The potential harms to the baby include increased rates of fetal growth restriction, preterm birth, and infant mortality.[6] Notably, there is strong evidence that protective antibodies are transmitted to infants whose mothers survive perinatal infection and breastfeed.[7] Vaccination therefore has a high likelihood of preventing severe COVID-19 infection and its adverse effects in both pregnant patients and their neonates.

The risks of administering COVID-19 vaccines during pregnancy appear to be minimal. Commonly reported side effects include short-term injection site pain, headache, fever, myalgia, arthralgia, chills, and nausea.[4] Although none of the vaccines currently in use have included pregnant patients in their clinical trials, the rate of serious adverse effects in study populations has been quite low.[4] Of the four vaccines being used in North America and Europe, none contain chemical components whose use is specifically contraindicated in pregnancy or breastfeeding.[4,5]

Patients who fear increased risk of miscarriage, congenital malformation, preterm delivery, or neonatal infection should be reassured that inactivated vaccines, such as the influenza vaccine, are frequently administered during pregnancy and have minimal risk of adverse events.[1] Severe allergic reactions to past vaccines or known allergies to any COVID-19 vaccine components are contraindications to being immunized.[4]

Current guidelines are mixed with respect to recommending or withholding COVID-19 vaccines in pregnant patients. The American College of Obstetrics and Gynecology asserts that in the absence of data showing that vaccines are contraindicated, pregnant patients should be immunized.[8] The Centers for Disease Control have taken a similar stance, noting that the only absolute contraindication to vaccination is having an allergy to vaccine components (Table).[4] However, the World Health Organization has more reserved guidelines,[9] stating that vaccination is only indicated in pregnant patients who are at high risk for exposure to COVID-19, such as health care workers, or those who have comorbidities that might make infection more severe.

It is important to consider that pregnancy itself is a comorbid condition that may increase the severity of COVID-19. Numerous immunological changes occur during gestation that modulate response to viral infection and may

Table. Vaccines currently being administered in North America and Europe

Vaccine name	Type	Dosage	Efficacy rate after full dose	Contraindication
Pfizer-BioNTech	mRNA	2 doses separated by 3 wk	95.0% (95% CI 90.3%–97.6%)[4]	Polyethylene glycol allergy
Moderna	mRNA	2 doses separated by 4 wk	94.1% (95% CI 89.3%–96.8%)[4]	Polyethylene glycol allergy
Janssen (Johnson & Johnson)	Adenoviral vector	1 dose	66.3% (95% CI 59.9%–71.8%)[4]	Polysorbate allergy
AstraZeneca[a]	Adenoviral vector	2 doses separated by 12 wk	81.2% (95% CI 60.3%–91.2%)[5]	Polysorbate allergy

[a] Not authorized for use in the United States.

contribute to more severe disease.[6] Reduction in chest volume and other pulmonary changes increase susceptibility to respiratory infections. Pregnancy also induces a hypercoagulable state that heightens the risk of thrombotic events, a known complication of SARS-CoV-2 infection.[6] Therefore, it is clear that from a physiological standpoint, severe COVID-19 poses a grave risk to the health of pregnant patients and their fetuses.

Because pregnant patients are more frequently exposed to outpatient and hospital environments during prenatal visits and delivery, it is reasonable to classify them as having a higher risk of COVID-19 exposure than the general population. Every pregnant patient then meets the World Health Organization criteria of being at high risk of exposure and at high risk for severe disease. Patients carrying pregnancies complicated by obesity, diabetes, or preeclampsia particularly stand to benefit from immunization against SARS-CoV-2. Prenatal vaccination is vital to prevent COVID-19 morbidity in the pregnant patient and to protect neonates via passive immunity.

With respect to scheduling, American College of Obstetrics and Gynecology and Centers for Disease Control guidelines recommend that patients wait at least 2 weeks after receiving any other immunization before receiving a COVID-19 vaccine.[4,8] Similar to influenza,[1] COVID-19 vaccination can be offered at any gestational age. Although antibody availability may be greatest for the neonate with vaccination later in gestation, maternal morbidity and mortality can occur throughout pregnancy. Vaccination thus confers the greatest benefit as soon as it is available to the mother and should not be delayed. For those attempting to become pregnant, there is no evidence that COVID-19 vaccines affect fertility, and vaccination need not be postponed.[4]

Although clinical trial data do not yet exist to verify the safety of COVID-19 vaccine use in pregnancy, precedent from past immunization efforts and the present pandemic provide strong support for vaccination. SARS-CoV-2 infection increases the likelihood of poor maternal and neonatal outcomes, which may be preventable with vaccination. In the absence of evidence that pregnancy is a contraindication, providers should make clear that the known benefits of receiving the vaccine far outweigh the unlikely potential harms. Obstetricians must continue to stay apprised of the literature surrounding vaccine safety and should counsel patients regarding individual fears and contraindications. As a population, pregnant patients have much to gain from immunization against COVID-19 and should be encouraged to take the vaccine.

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