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Pregnancy should be a condition eligible for additional doses of COVID-19 messenger RNA vaccines

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Vaccines against COVID-19 have been successful in preventing severe illness and death; however, given the emergence of new variants along with waning immunity from both vaccinations and previous infections, booster doses of the vaccines have been widely recommended. Currently, the Centers for Disease Control and Prevention (CDC) recommends a bivalent booster vaccination for all persons ≥5 years of age if it has been ≥2 months since their last vaccine dose (either completion of their primary series or monovalent booster). It is expected that annual booster vaccinations will be recommended for the general public, although at-risk groups may be eligible for boosters more frequently. For example, in March 2022, the CDC recommended offering a second monovalent vaccine booster dose 4 months after the first booster to high-risk persons, defined as those aged ≥50 years and aged ≥12 years with moderate or severe immunocompromised health conditions; pregnancy alone was not an indication for an additional booster. Given the risk of COVID-19 in pregnant persons and their fetuses or infants, we believe that additional booster doses should be offered to pregnant individuals who received a bivalent COVID-19 booster before becoming pregnant.

EDITOR'S CHOICE

COVID-19 presents a risk to pregnant individuals and their fetuses. Pregnancy is a known risk factor for complications from COVID-19; pregnant persons are more likely to be admitted to intensive care units, to require invasive ventilation, to receive extracorporeal membrane oxygenation, and to die than nonpregnant women of reproductive age. Moreover, the neonatal period and initial months of life are times of increased COVID-19 risk. More COVID-19–attributed deaths have been recorded in persons <6 months of age than any other pediatric age group in the United States; as of July 13, 2022, infants aged 0 to 5 months (who are not yet eligible for vaccination) account for 20% (225/1125) of US COVID-19–associated pediatric deaths (https://data.cdc.gov/NCHS/Provisional-COVID-19-Death-Counts-by-Age-in-Years-/3apk-4u4f).

Existing literature indicates that COVID-19 vaccines administered during pregnancy provide substantial protection to mothers and fetuses. However, in a study examining pregnant persons vaccinated in the first trimester of pregnancy, antibody waning was observed; boosting increased maternal and neonatal antibody levels when third-trimester booster doses were provided.[1] A recent analysis showed that neutralizing antibodies against the omicron variant were absent at delivery after receipt of 2-dose series; a third booster dose was necessary to provide neutralizing antibody protection against omicron to mothers and neonates.[2] In addition, a recent analysis of COVID-19–associated hospitalization among infants <6 months of age showed that vaccination of mothers at >20 weeks of gestation had higher effectiveness than when given earlier in pregnancy (69% vs 38%).[3] Administering vaccinations later in pregnancy may maximize benefits by conferring protection later in pregnancy while maximizing the effective subsequent magnitude and duration of protection offered to fetuses by placental antibody transfer.

Concurrently, no evidence of harm from third or additional doses of COVID-19 messenger RNA (mRNA) vaccines in females in the demographic of childbearing potential exists. Moreover, data continue to accumulate regarding the safety of COVID-19 vaccines during pregnancy for fetuses and newborns. Although data are limited regarding booster doses during pregnancy, we believe that it is unlikely that additional appropriately spaced doses pose

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threats to maternal or infant health, especially weighed against the benefits of protection against COVID-19 provided to mothers and newborns.

The concept that maternal vaccination protects infants with placentally transferred passive immunity is not new. In developing countries, tetanus toxoid vaccination is used to protect infants from neonatal tetanus. Inactivated influenza vaccination during pregnancy has been shown to protect mothers and infants for up to 6 months of life. The tetanus toxoid, reduced diphtheria toxin, and acellular pertussis (Tdap) vaccine is recommended for pregnancy during the early part of gestational weeks 27 to 36 to maximize protection of infants from pertussis during the first months of life when risks are the highest.

The paucity of data on risks during pregnancy of different medications and vaccines presents a frequent dilemma as pregnancy is often an exclusion for clinical trials of new medications and vaccines. This means that limited safety data are available for most medications at the time of initial marketing. Clinicians are left to weigh the benefits of the medication against unknown potential risks. The same is true for public health decision-making regarding interventions for pregnant persons. For example, during the 2009 H1N1 pandemic, after carefully weighing the benefits of preventing severe maternal illness against the potential risks of oseltamivir, the CDC recommended oseltamivir for all pregnant persons with known or suspected influenza, even though the potential risks of oseltamivir to the fetus were largely unknown. Similarly, when the initial recommendation for Tdap vaccine was extended to every pregnancy, the effects of repeated vaccination in subsequent pregnancies were not fully understood but were believed to be outweighed by the substantial protection provided to infants during the first few months of life from pertussis. Both interventions have been shown to have benefits—protection of the mother from severe complications from influenza with oseltamivir treatment and protection of the infant from pertussis infection and hospitalization with maternal Tdap vaccination—without evidence of increased risks.[4,5]

In summary, we have an intervention that seems poised to substantially reduce morbidity and mortality in pregnant persons and their infants; however, additional doses of COVID-19 vaccines are not currently recommended during pregnancy. All pieces of evidence suggest that pregnant persons are at increased risk. Moreover, they are carrying fetuses that will, after birth, enter a group that could have higher risks of COVID-19–associated morbidity and mortality than some individuals in groups currently eligible for additional doses under the current policy. A rigorous, transparent, and public assessment of all available data regarding the benefits and potential risks of this proposed strategy would, in our view, likely lead the Food and Drug Administration to authorize and the CDC to recommend that pregnant people receive an additional dose of mRNA COVID-19 vaccine, if they are >4 months from their most recent dose, whether primary series or booster. Such assessments will benefit from additional outcomes data. Although the timing of additional doses can be debated, doses offered after 20 weeks of gestation seem likely to be optimal in most circumstances. If enacted, this policy change would address an important gap in protection for 2 important and vulnerable populations. ■

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