# Infections in Pregnancy and the Role of Vaccines



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#### **KEYWORDS**

- Influenza Pertussis Zika Influenza vaccine Tdap vaccine
- Maternal vaccination

#### **KEY POINTS**

- The Advisory Committee of Immunization Practices recommends administration of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis with each pregnancy and inactivated influenza vaccine in influenza season.
- There are other vaccines that may (or should) be used in pregnancy under certain circumstances.
- As women's health providers, we have come a long way in the arena of maternal vaccination, and continued research is paramount.

#### INTRODUCTION

Infectious disease remains a major cause of mortality worldwide, but before the advent of modern medicine, was the leading cause of mortality in the United States.<sup>1</sup> The 3 leading causes of death reported in 1900 in America were pneumonia, tuberculosis, and diphtheria, causing one-third of all deaths.<sup>1</sup> Between 1900 and 2000, the life expectancy for a person born in the United States increased from 47.3 to 76.8 years<sup>1</sup> with decreased mortality attributed in part to advances in vaccinology.<sup>2</sup> Avoidance of

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Conflicts of Interest: G.K. Swamy is on a Data and Safety Monitoring Board for a GlaxoSmithKline-funded respiratory syncytial virus (RSV) vaccine study in pregnant women. She has received research funding for studies of group B streptococcus vaccine in pregnant women produced by Novartis and for RSV vaccine in pregnant women produced by Novavax. K.B. Fortner has received research funding for studies of group B streptococcus vaccine in pregnant women produced by Novartis and for RSV and cytomegalovirus surveillance among pregnant women and their infants by Pfizer and Regeneron. The remaining authors have no conflicts of interest to declare.

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millions of deaths are attributed to expanded coverage of measles, polio, and, more recently, pneumococcal vaccines.<sup>2</sup>

At present, 17 vaccine-preventable diseases are covered by 14 routine vaccines, 2 of which are recommended during most pregnancies.<sup>3</sup> Starting in 1997, the Centers for Disease Control and Prevention's (CDC) Advisory Committee of Immunization Practices (ACIP) recommended annual vaccination against influenza in all women pregnant during influenza season.<sup>4</sup> In October of 2012, the tetanus–diphtheria–acellular pertussis vaccine was recommended in pregnancy in response to increased rates of pertussis infection.<sup>5,6</sup> Pregnant women are at risk for infection just as their nongravid counterparts and, in some cases, may have more significant morbidity and mortality than their peers.<sup>7,8</sup> This review outlines the following:

- 1. Maternal immunization and types of immunizations,
- 2. Immunizations recommended during pregnancy,
- 3. Conditional vaccines to be considered,
- 4. Research frontiers in immunization, and
- 5. The role of obstetrician/gynecologists as vaccinators.

#### MATERNAL IMMUNIZATION BENEFITS

Maternal immunization is a purposeful, successful strategy to prevent or mitigate the severity of infections in pregnant women and their newborn infants. The prevention of illness during pregnancy impacts the health care system 2-fold by keeping the mother–infant dyad intact and healthy.<sup>9</sup> For example, flu vaccinated pregnant women seem to have longer pregnancies with larger neonates.<sup>10,11</sup> Pregnancy, by virtue of innate physiologic changes, increases a woman's susceptibility to illness.<sup>7</sup> Ensuing flu seasons have revealed that infected pregnant women have higher rates of hospitalization, cardio-pulmonary complications, and death compared with the general public.<sup>8,12,13</sup> Pregnancy increases a woman's exposure to the health care system and to a provider with whom she can build a relationship, giving time for education, planning, vaccine administration, and follow-up.<sup>9</sup> The majority of pregnant women report visits to their obstetric provider more than 6 times during pregnancy, allowing many opportunities to discuss and give vaccines.<sup>12</sup> Immunization in pregnancy also seems to have maternal, neonatal, and obstetric benefit, with several studies showing improved birth outcomes.<sup>10,14</sup>

### Types of Vaccines

Pregnancy modulates the baseline immune response in a protective effort to diminish an inflammatory reaction to the fetus.<sup>7</sup> A shift occurs from T-helper cells, which produce cytokines that facilitate pregnancy loss, to T-helper 2 cells, which render and permit fetal antigen tolerance.<sup>7</sup> This modulatory effect diminishes maternal protection, yielding gravid women vulnerable compared with their nongravid counterparts as evidenced by the 1918, 1959, and 2009 pandemic flu seasons.<sup>15–17</sup> In the 2009 pandemic, pregnant women were 4 times more likely to be hospitalized secondary to flu-related complications and represented 5% of flu-related mortalities despite only representing 1% of the US population.<sup>16</sup> Thus, vaccination can help to combat the disproportionate representation of pregnant women in morbidity and mortality statistics.

Vaccines are categorized into 2 basic groups: inactivated or live attenuated (**Table 1**). Inactivated vaccines consist of a component of the infectious pathogen rendered incapable of causing clinical disease. For example, the tetanus vaccine contains the tetanus toxoid, which is produced by *Clostridium tetani*. As such, the pathogen is not introduced, but produces a humoral immune response to the toxoid, conferring immunity. Other types of components used in vaccines include whole

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