Should we stop administering the influenza vaccine to pregnant women?

**No.** Although a recent case-control study found that the odds ratio of spontaneous abortion in women who received the pH1N1 vaccine (a vaccine that differs from the current quadrivalent vaccine) 2 years in a row was 6.5, compared with 1.3 in women who were not vaccinated with the pH1N1 vaccine in 2 consecutive seasons, more research is needed. ACOG and the CDC advise the continued practice of routinely offering the influenza vaccine to virtually all pregnant women at the beginning of the flu season.


**EXPERT COMMENTARY**

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Influenza can be a serious, even life-threatening infection, especially in pregnant women and their newborn infants. For that reason, the Centers for Disease Control and Prevention (CDC) and the American College of Obstetricians and Gynecologists (ACOG) strongly recommend that all pregnant women receive the inactivated influenza vaccine at the start of each flu season, regardless of trimester of exposure.

The most widely-used vaccine in the United States is the inactivated quadrivalent vaccine, which is intended for intramuscular administration in a single dose. The 2017–2018 version of this vaccine includes 2 influenza A antigens and 2 influenza B antigens. The first of the A antigens differs from last year’s vaccine. The other 3 antigens are the same as in the 2016–2017 vaccine:
- A/Michigan/45/2015 (H1N1) pdm09-like virus
- A/Hong Kong/4801/2014 (H3N2)-like virus
- B/Brisbane/60/2008-like virus
- B/Phuket/3073/2013-like virus (B/Yamagata).

Several recent reports in large, diverse populations have demonstrated that the vaccine does not increase the risk of spontaneous abortion, stillbirth, preterm delivery, or congenital anomalies. Therefore, a recent report by Donahue and colleagues is surprising and worthy of our attention.

**Details of the study**

Donahue and colleagues, experienced investigators, were tasked by the CDC with using information from the Vaccine Safety Datalink to specifically assess the safety of the influenza vaccine when administered early in pregnancy. They evaluated
485 women who had experienced a spontaneous abortion in 1 of 2 time periods: September 1, 2010 to April 28, 2011 and September 1, 2011 to April 28, 2012. These women were matched by last menstrual period with controls who subsequently had a liveborn infant or stillbirth at greater than 20 weeks of gestation. The exposure of interest was receipt of the monovalent H1N1 vaccine (H1N1pdm09), the inactivated trivalent vaccine (A/California/7/2009 H1N1-pdm09-like, A/Perth/16/2009 H3N2-like, and B/Brisbane/60/2008-like), or both in the 28 days immediately preceding the spontaneous abortion. The investigators also considered 2 other windows of exposure: 29 to 56 days and greater than 56 days. In addition, they controlled for the following potential confounding variables: maternal age, smoking history, presence of type 1 or 2 diabetes, prepregnancy body mass index (BMI), and previous health care utilization.

Cases were significantly older than controls. They also were more likely to be African-American, to have had a history of greater than or equal to 2 spontaneous abortions, and to have smoked during pregnancy. The median gestational age at the time of spontaneous abortion was 7 weeks. Overall, the adjusted odds ratio (aOR) of spontaneous abortion within the 1- to 28-day window was 2.0 (95% confidence interval [CI], 1.1–3.6). There was not even a weak association in the other 2 windows of exposure. However, in women who received the pH1N1 vaccine in the previous flu season, the aOR was 7.7 (95% CI, 2.2–27.3). When women who had experienced 2 or more spontaneous abortions were excluded, the aOR remained significantly elevated at 6.5 (95% CI, 1.7–24.3). The aOR was 1.3 (95% CI, 0.7–2.7) in women who were not vaccinated with the pH1N1 vaccine in the previous flu season.

Donahue and colleagues offered several possible explanations for their observations. They noted that the pH1N1 vaccine seemed to cause at least mild increases in pro-inflammatory cytokines, particularly in pregnant compared with nonpregnant women. In addition, infection with the pH1N1 virus or vaccination with the pH1N1 vaccine induces an increase in T helper type-1 cells, which exert a pro-inflammatory effect. Excessive inflammation, in turn, may cause spontaneous abortion.

**Study limitations**

This study has several important limitations. First, the vaccine used in the investigation is not identical to the one used most commonly today. Second, although the number of women with spontaneous abortions is relatively large, the number who received the pH1N1 virus or vaccination with the pH1N1 vaccine induces an increase in T helper type-1 cells, which exert a pro-inflammatory effect. Excessive inflammation, in turn, may cause spontaneous abortion.

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References


