Influenza vaccine in pregnancy: Is it safe?

Influenza vaccine has been administered to pregnant women since the 1950s, initially to those with high-risk medical conditions such as chronic heart or lung disease and later to health care workers. Since the 1990s, use in pregnancy has been expanded more broadly in many countries in recognition of the risk of influenza-related complications and benefits to both mother and infant, with even higher rates of use in pregnancy during the 2009 A/H1N1 pandemic because of severity of the infection in pregnancy. In the United States, influenza vaccine coverage in pregnant women has exceeded 50% since the 2009–10 season,[1] and while seasonal uptake data in pregnancy are not available in Canada, coverage among pregnant women in BC during the 2009 pandemic A/H1N1 campaign was 54%.

Inactivated influenza vaccine is recommended for all pregnant women at any stage of pregnancy during the influenza season, typically from November through April each year.[2,3] Benefits include maternal protection against influenza-associated morbidity, including hospitalization for cardiopulmonary complications, the rate of which progressively increases with duration of the pregnancy and is maximal in the third trimester. Maternal immunization is also associated with reduced risk of influenza and associated hospitalization of the infant, and infants born to vaccinated women have lower rates of prematurity, low birth weight, and being small for their gestational age.[4] Protection of the infant occurs through two mechanisms: directly through passive transfer of humoral immunity from the mother in utero, and indirectly through cocooning by immunization of close household contacts and caregivers. Direct protection by infant vaccination is not achievable with current vaccines prior to 6 months of age.

Inactivated influenza vaccine is recommended for all pregnant women at any stage of pregnancy during the influenza season, typically from November through April each year.

Historically, both drugs and vaccines have been used sparingly in pregnancy. Avoidance of vaccines has been largely based on theoretical concerns about teratogenicity of live vaccines such as rubella and varicella, which have not been borne out. A secondary consideration for avoiding vaccines has been that an anomaly will be misattributed to vaccine, especially if received in the first trimester. Influenza vaccination during pregnancy is associated with a brief increase in maternal inflammatory biomarkers, but this response is not associated with fetal development and risk of congenital anomalies.[5] At its June 2013 meeting, the World Health Organization Global Advisory Committee on Vaccine Safety concluded from their review of vaccine safety in pregnancy that there is no evidence of adverse pregnancy outcomes from vaccination in pregnancy with inactivated virus (including influenza), bacterial, or toxoid vaccines.[6,7]

The historical precautionary approach to use of vaccines in pregnancy and over two decades of recommendations for influenza vaccination in pregnancy mean that much of the data on influenza vaccine safety in pregnancy originate from observational studies, including database reviews and postmarketing surveillance, instead of randomized trials; nevertheless, these have concluded that influenza vaccine is safe during pregnancy, including multidose products containing thimerosal as a preservative.[8-10] Additionally, many more recent studies have been conducted and several reviews of the literature have been published since 2009, assessing both 2009 pandemic A/H1N1 and seasonal inactivated influenza vaccines. These studies and reviews have examined the occurrence of preterm birth, fetal death, stillbirth, spontaneous abortion, and congenital malformations.[11-13] These reviews have found an overall lack of association between influenza vaccine receipt and adverse pregnancy outcomes, and physicians can confidently reassure pregnant women about safety of influenza vaccines in pregnancy. Review authors commented on the need to define standards for future studies of vaccine safety in pregnancy to ensure consistently defined end points; for instance, fetal death was variably defined in studies at gestations ranging from over 12 to over 25 weeks or over 500 grams. To this end the US National Institutes of Health convened an international consensus conference on harmonized safety monitoring of immunization in pregnancy in late March 2016. Development of standards should pave the way for more consistent reporting of results from future studies, including pooling of results for meta-analyses. This is increasingly important because of

This article is the opinion of the BC Centre for Disease Control and has not been peer reviewed by the BCMJ *Editorial Board.*

greater future use of vaccines in pregnancy beyond influenza, including for prevention of pertussis, group B streptococcal disease, and respiratory syncytial virus infections.

—Monika Naus, MD, MHSc, FRCPC
Medical Director, Immunization Programs and Vaccine Preventable Diseases Service

References

1. Groom HC, Henninger ML, Smith N, et al. Influenza vaccination during pregnancy: Influenza seasons 2002-2012, Vaccine Safety Datalink. Am J Prev Med 2016; 50:480-488.
2. BCCDC. Communicable disease control manual. Chapter 2, Immunization. Section VII, Biological products. Accessed 3 August 2016. www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization.
3. National Advisory Committee on Immunization (NACI). Public Health Agency of Canada. An advisory committee statement (ACS). Canadian immunization guide chapter on influenza and statement on seasonal influenza vaccine for 2016-2017. Accessed 3 August 2016. www.phac-aspc.gc.ca/naci-ccni/flu-2016-grippe-eng.php.
4. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. N Engl J Med 2008;359:1555-1564.
5. DeSilva M, Munoz FM, Mcmillan M, et al. Congenital anomalies: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine 2016;pii:S0264-410X(16)30030-5.
6. World Health Organization. Global Advisory Committee on Vaccine Safety, 12-13 June 2013. Wkly Epidemiol Rec 2013; 88:301-312.
7. Keller-Stanislawski B, Englund JA, Kang G, et al. Safety of immunization during pregnancy: A review of the evidence of selected inactivated and live attenuated vaccines. Vaccine 2014;32:7057-7064.
8. Tamma PD, Ault KA, del Rio C, et al. Safety of influenza vaccination during pregnancy.AmJObstetGynecol2009;201:547-552.
9. Bednarczyk RA, Adjaye-Gbewonyo D, Omer SB. Safety of influenza immunization during pregnancy for the fetus and the neonate. Am J Obstet Gynecol 2012;207 (3 suppl):S38-46.
10. Munoz FM. Safety of influenza vaccines in pregnant women. Am J Obstet Gynecol 2012;207(3 suppl):S33-37.
11. Fell DB, Platt RW, Lanes A, et al. Fetal death and preterm birth associated with maternal influenza vaccination: Systematic review. BJOG 2015;122:17-26.
12. McMillan M, Porritt K, Kralik D, et al. Influenza vaccination during pregnancy: A systematic review of fetal death, spontaneous abortion, and congenital malformation safety outcomes. Vaccine 2015;33:2108-2117.
13. Bratton KN, Wardle MT, Orenstein WA, Omer SB. Maternal influenza immunization and birth outcomes of stillbirth and spontaneous abortion: A systematic review and meta-analysis. Clin Infect Dis 2015;60:e11-19.

pulsimeter

Continued from page 407

Rudzicz is also a scientist at Toronto Rehab-University Health Network. Regulatory approval will be sought in Canada and the United States to make the technology available to family doctors and speech-language pathologists.

Ten teams from Canada and around the world competed in the AGE-WELL Pitch Competition, which showcased a variety of technology solutions that address the challenges faced by people living with dementia.