Evidence file on the safety of flu vaccine use during pregnancy

Recommendations from other countries on the use of H1N1v flu vaccines during pregnancy

- Australia – Department of Health and Ageing
- Canada – Statement from the Society of Obstetricians and Gynaecologists and the Public Health Agency of Canada
- Ireland – Statement from the Institute of Obstetricians & Gynaecologists of the Royal College of Physicians of Ireland
- US – Letter from the American Academy of Family Physicians / American College of Obstetricians and Gynecologists / American Medical Association / Centres for Disease Control and Prevention

Papers on the effects of the flu vaccine during pregnancy

Is routine influenza immunization warranted in early pregnancy?
Skowronski DM, De Serres G.
BC Centre for Disease Control, Vancouver, BC, Canada.
Routine influenza immunization is recommended for select groups because of their higher risk of serious influenza outcomes. Based on that benefit-risk framework, we assessed whether routine administration of trivalent inactivated influenza vaccine (TIV) is warranted in pregnancy, beginning in 1st trimester. Higher maternal mortality due to influenza was extensively described during the 1918 and 1957 pandemics, but epidemiologic evidence thereafter is limited to case reports and a single ecologic analysis during a single season. Significantly elevated rates of hospitalization have been reported with seasonal influenza beginning in 1st trimester among women with select comorbidities and during the 2nd half of normal pregnancy. TIV protection against serious outcomes in pregnant women has not yet been shown. Although harm has also not been shown, sample size to date is insufficient to assert TIV safety in 1st trimester. Benefit-risk analysis suggests influenza immunization may be warranted at any stage of pregnancy during certain pandemics and annually among women with select comorbidities. TIV may also be warranted to protect women against influenza-related hospitalization during the 2nd half of normal pregnancy. Evidence is otherwise insufficient to recommend routine TIV as the standard of practice for all healthy women beginning in early pregnancy.

Influenza vaccination in pregnancy: current evidence and selected national policies.
Mak TK, Mangtani P, Leese J, Watson JM, Pfeifer D.
Department of Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland.
In several countries, pregnant women are recommended seasonal influenza vaccination and identified as a priority group for vaccination in the event of a pandemic. We review the evidence for the risks of influenza and the risks and benefits of seasonal influenza vaccination in pregnancy. Data on influenza vaccine safety in pregnancy are inadequate, but the few published studies report no serious side-effects in women or their infants, including no indication of harm from vaccination in the first trimester. National policies differ widely, mainly because of the limited data available, particularly on vaccination in the first trimester. The evidence of excess morbidity during seasonal influenza supports vaccinating healthy pregnant women in the second or third trimester and those with comorbidities in any trimester. The evidence of excess mortality in two previous influenza pandemics supports vaccinating in any trimester during a pandemic.

Effectiveness of maternal influenza immunization in mothers and infants.
Zaman K, Roy E, Arifeen SE, Rahman M, Raqib R, Wilson E, Omer SB, Shahid NS, Breiman RF, Steinhoff MC.
Effectiveness of influenza vaccine during pregnancy in preventing hospitalizations and outpatient visits for respiratory illness in pregnant women and their infants.

Black SB, Shinefield HR, France EK, Fireman BH, Platt ST, Shay D; Vaccine Safety Datalink Workgroup.

Kaiser Permanente Vaccine Study Center, Oakland, CA 94612, USA.

The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention recommends influenza vaccination for women who will be in the second or third trimester of pregnancy during the influenza season. We analyzed hospital admissions with principal diagnoses of influenza or pneumonia and influenza-like illness (ILI) outpatient visits to study the effectiveness of influenza vaccine during pregnancy in protecting women and infants from influenza-related morbidity. Estimates of influenza vaccine effectiveness across five flu seasons (Fall 1997 to Spring 2002) were calculated using Cox proportional hazards models for women and infant study populations in Kaiser Permanente Northern California. Outpatient utilization outcomes included physician visits with a diagnosis of upper respiratory infection, pharyngitis, otitis media, asthma, bronchial asthma, viral infection, pneumonia, fever, cough, or wheezing associated with respiratory illness. Inpatient outcomes included hospitalizations with principal diagnoses of influenza or pneumonia. Women who received influenza vaccine during pregnancy had the same risk for ILI visits compared with unvaccinated women, adjusting for women's age and week of delivery. When asthma visits were excluded from the outcome measure, we also found no difference in the risk of outpatient visits for vaccinated and unvaccinated women. Hospital admissions for influenza or pneumonia in women in the study population were quite rare and no women died of respiratory illness during pregnancy. Infants born to women who received influenza vaccination had the same risks for influenza or pneumonia admissions compared with infants born to unvaccinated women, adjusting for infant's gender, gestational age, week of birth, and birth facility. Maternal influenza vaccination was also not a significant determinant of risk of ILI (excluding otitis media) outpatient visits for infants, nor did it significantly affect the risk of otitis media visits. Influenza vaccination during pregnancy did not significantly affect the risk of cesarean section, adjusting for the woman's age. It also did not affect the risk of preterm delivery. Although the immunogenicity of influenza vaccination in pregnancy in mother and infant has been well documented, in this study, we were unable to demonstrate the effectiveness of influenza vaccination with data for hospital admissions and physician visits. One possible interpretation of these findings is that typical influenza surveillance measures based on utilization data are not reliable in distinguishing influenza from other respiratory illness. Hospitalizations for respiratory illness were uncommon in both vaccinees and nonvaccinees.


Antigen-specific immune responses to influenza vaccine in utero.

Initial immune responses to allergens may occur before birth, thereby modulating the subsequent development of atopy. This paradigm remains controversial, however, due to the inability to identify antigen-specific T cells in cord blood. The advent of MHC tetramers has revolutionized the detection of antigen-specific T cells. Tetramer staining of cord blood after CMV infection has demonstrated that effective CD8(+) antigen-specific immune responses can follow intrauterine viral infections. We hypothesized that sensitization to antigens occurs in utero in humans. We studied cord blood B and T cell immune responses following vaccination against influenza during pregnancy. Anti-Fluzone and anti-matrix protein IgM antibodies were detected in 38.5% (27 of 70) and 40.0% (28 of 70), respectively, of cord blood specimens. Using MHC tetramers, HA-specific CD4(+) T cells were detected among 25.0% (3 of 12) and 42.9% (6 of 14) of cord blood specimens possessing DRB1*0101 and DRB1*0401 HLA types, respectively, and were detected even when the DRB1 HLA type was inherited from the father. Matrix protein-specific CD8(+) T cells were detected among 10.0% (2 of 20) of HLA-A*0201(+) newborns. These results suggest that B and T cell immune responses occur in the fetus following vaccination against influenza and have important implications for determining when immune responses to environmental exposures begin.

Immunization of pregnant women with influenza A/New Jersey/76 virus vaccine: reactogenicity and immunogenicity in mother and infant.
Sumaya CV, Gibbs RS.
The safety and immunogenicity of inactivated influenza virus vaccines in pregnant women have not been adequately investigated. In this study, 56 women received inactivated influenza A/New Jersey/76 virus vaccine during the second and third trimesters of pregnancy. No significant immediate reactions or increased fetal complications were associated with administration of the vaccine. The antibody response of the pregnant women to the vaccine was similar to that of nonpregnant adults. Forty mother-infant pairs were available for antibody surveillance. At delivery, reciprocal antibody titers of greater than or equal to 20 were present in 11 (42%) newborn (cord) sera and 15 (58%) maternal sera. Three months later, sera from only three infants (12%) contained this level of antibody. At six months, the serum of only one infant contained this level of antibody. At six months, the serum of only one infant contained detectable antibodies. Levels of passively transferred antibodies from prior maternal infection with influenza A/Victoria/75 virus also declined rapidly following birth. It is possible that immunization of pregnant women can provide sufficient protection of the newborn infants by transfer of antibodies through the placenta if (1) a more potent influenza vaccine, possibly used with booster dosing, is administered, and (2) the women deliver just prior to or during the influenza season.

Protection of infants from infection with influenza A virus by transplacentally acquired antibody.
Puck JM, Glezen WP, Frank AL, Six HR.
Transplacentally acquired antibody to influenza A virus was measured by a microneutralization test and a radioimmunoprecipitation assay in cord blood obtained from infants at a large urban county hospital in 1975-1978. Random samples tested before epidemic periods were a measure of susceptibility of the population. Twenty-six infants from whom cord sera were available had culture-documented infections with influenza A/Victoria (H3N2) virus when younger than four months. The direct correlation between age at the time of infection and level of antibody measured in cord serum (P less than 0.002) suggested a protective effect of transplacentally acquired antibody. None of fourteen acute-phase serum specimens obtained early in the course of culture-positive infections of young infants had detectable antibody to influenza A viral hemagglutinin by the sensitive radioimmunoprecipitation test. Because passively transferred maternal antibody to influenza virus may prevent symptomatic infection in young infants, vaccination of pregnant women could be beneficial.

8: J Infect Dis. 1993 Sep;168(3):647-56.
Maternal immunization with influenza or tetanus toxoid vaccine for passive antibody protection in young infants.
Englund JA, Mbawuike IN, Hammill H, Holleman MC, Baxter BD, Glezen WP.
Dept. of Microbiology and Immunology, Baylor College of Medicine, Houston, TX 77030.
Women in the last trimester of pregnancy were given trivalent inactivated influenza virus vaccine (TIV; A/Sichuan/H3N2, A/Taiwan/H1N1, B/Victoria) or tetanus toxoid (TT). Maternal blood was drawn
before immunization and at delivery (median, 5 weeks later); infant blood was obtained within 5 days of birth and 2 months later. Antibody responses to TIV and TT were determined by microneutralization assay and ELISA. T cell response was determined by lymphocyte proliferation. Maternal seroconversion to vaccine antigens was found to one or more influenza antigen in all TIV recipients and to TT in 9 of 13 TT recipients. Significantly higher IgG antibodies to maternal vaccine antigens were present in cord and infant serum. Significant blastogenic responses were seen to influenza A and B in maternal cells of TIV-immunized women but not in cord or infant lymphocytes. Maternal immunization resulted in higher infant levels of vaccine-specific IgG antibody but not in the transfer of specific T lymphocyte response(s) or production of neonatal IgM antibody.

Last updated 26 October 2009