Prevention and Management of Influenza in Pregnancy

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KEYWORDS

• Influenza • Pregnancy • Influenza vaccine

KEY POINTS

- Pregnancy increases the risk for severe disease, hospitalization, and mortality from influenza infection.
- In addition to negative effects on the mother, influenza infection is associated with untoward pregnancy outcomes such as preterm birth and small-for-gestational-age infants.
- Immunization with the inactivated influenza vaccine is the most effective way to prevent influenza infection, and all pregnant women lacking contraindication should be immunized against influenza.
- Antiviral medications have been found to reduce the risk of influenza infection after exposure and the severity and duration of infection among those infected. Obstetric providers should have a low threshold for use of the neuraminidase inhibitors for prevention and treatment of influenza in pregnancy.

INTRODUCTION AND EPIDEMIOLOGY

Influenza has been known to cause recurrent worldwide epidemics of febrile respiratory disease for at least 400 years. In this approximate period, records indicate that we have experienced at least 31 influenza pandemics. The most severe recorded influenza pandemic was the 1918 to 1919 "Spanish flu," with estimates of global mortality of at least 20 million. Looking specifically at the effects of the Spanish flu in the United

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States, more than 500,000 attributable deaths were recorded in the United States during a span of 1.5 years.[1]

Influenza is an ongoing source of human morbidity and mortality. The latest Centers for Disease Control and Prevention (CDC) estimates suggest that domestic annual attributable mortality from seasonal influenza infection alone varies from 3000 to more than 49,000 per year, depending on strain specifics and additional variables.[2] In addition to mortality, the estimated 25 to 50 million cases of domestic seasonal influenza are responsible for millions of days of illness with work and school absenteeism and more than 200,000 annual influenza-related hospitalizations.[3] The combined direct medical costs and lost income related to seasonal influenza disease are significant at an estimated $26.8 billion annually in the United States.[4] Importantly, pregnancy is one of a few recognized clinical conditions that increase risk of hospitalization, serious complications, and death from influenza infection.

Influenza viruses are enveloped, single-stranded, RNA viruses in the Orthomyxoviridae family. Influenza viruses are further divided into influenza virus types A, B, and C based on particular antigenic profiles. Although all 3 influenza types have been implicated in human disease, influenza A and B strains cause most human infections. Thus, influenza A and B are the primary focus of clinical prevention and treatment efforts on a yearly basis. Additionally, thus far, only type A has been associated with the occasional influenza pandemic. Additional subdivision into serotypes is done based on their surface proteins, hemagglutinin (HA) and neuraminidase (NA). Currently, 16 different HA glycoproteins (H1–H16) and 9 NA serotypes (N1–N9) have been identified. This large number of strains contributes to the well-known influenza strain variability.

Importantly, these surface glycoproteins are important for viral entry into and exit from epithelial cells lining the human respiratory tract and are the basis of the H and N naming designations for all influenza strains (ie, H1N1 or H3N2).[1] Briefly, the HA protein mediates binding to extracellular receptors, facilitating fusion of viral and host membranes, and the NA protein acts on sialic acid residues on the surface of host cells to direct release of newly synthesized viral particles.[1,5] These viral particles go on to infect new host cells, thus, propagating the systemic infection. Respectively, these 2 proteins are the current pharmacologic targets of the 2 classes of anti-influenza medications, the adamantanes (eg, amantadine and rimantadine) and neuraminidase inhibitors (eg, oseltamivir and zanamivir). Since 2009, the adamantanes are no longer recommended for general use because of concerns about large-scale resistance among circulating influenza viruses.[6]

Influenza is also appreciated for its ongoing and naturally occurring viral alterations and mutations. These ongoing viral changes are what generate the altered antigenic characteristics, in turn, driving the necessity of yearly alterations to vaccine composition (antigenic drift). Similar antigenic differences, yet more dramatic and fundamental, are what give rise to the occasional influenza pandemic (antigenic shift). Antigenic drift is the perpetually ongoing process of modest antigenic alterations producing antigenic structures different enough for immune memory evasion. This occurs in all influenza subtypes and is responsible for yearly epidemics and the concomitant need for yearly considerations of the relevance and potential disease prevention impact of vaccine formulations. Antigenic shift is a much rarer occurrence (but nevertheless part of the natural influenza lifecycle) when 2 or more different influenza strains combine to produce a novel antigenic structure that has negligible recognition within the population. This process is currently known to occur only in influenza A viruses and happens approximately once every 20 to 30 years. This rare, yet ongoing occurrence is what produces the occasional influenza pandemic, such as the 2009 H1N1 pandemic. These “new” characteristics of the viral surface structure generated from antigenic