

Attention: HIV-infected pregnant women are at risk of potentially serious disease due to influenza viruses. The Centers for Disease Control and Prevention (CDC) recommends that pregnant women, including HIV-infected pregnant women, with confirmed, probable, or suspected novel influenza A (H1N1) infection receive antiviral therapy with oseltamivir (Tamiflu).

Pregnant Women and Novel Influenza A (H1N1): Considerations for Clinicians

Summary

Pregnancy raises risk for complications related to seasonal as well as pandemic influenza infections such as those caused by the novel influenza A (H1N1) virus. The CDC has recently summarized information about novel H1N1 infection during pregnancy and has issued preliminary treatment recommendations, shown below (May 7, 2009 4:35 PM ET URL: http://www.cdc.gov/h1n1flu/clinician_pregnant.htm).

Twenty cases of novel H1N1 (15 confirmed and 5 probable) in pregnant women have been reported in the U.S. as of May 10, 2009. Three women were hospitalized, and one of them died. Based on available data, the CDC recommends that pregnant women with confirmed, probable, or suspected novel H1N1 infection receive antiviral therapy with oseltamivir (Tamiflu; preferred for its systemic absorption) for 5 days. Therapy should be initiated as soon as possible, even if more than 48 hours have elapsed since symptom onset. Acetaminophen should also be administered, as fevers are associated with adverse maternal and fetal outcomes. Pregnant women who have had close contact with someone who has confirmed, probable, or suspected novel H1N1 infection should receive prophylaxis with either oseltamivir or zanamivir (Relenza) for 10 days.

Both the [Advisory Committee on Immunization Practices](#) and the [American College of Obstetricians and Gynecologists](#) recommend annual influenza vaccination for all pregnant women. However, because the 2008–2009 seasonal vaccine does not protect against novel H1N1, even vaccinated pregnant women with flu-like symptoms should be evaluated and treated. Although the safety and efficacy of oseltamivir during pregnancy have not been firmly established, the benefits of this antiviral drug are likely to outweigh the risks. Novel H1N1 seems to be resistant to amantadine and rimantadine, so these drugs should not be used in people with suspected novel H1N1 infection.

Background

Human infections with a novel influenza A (H1N1) virus that is easily transmissible among humans were first identified in April 2009. The epidemiology and clinical presentations of these infections are currently under investigation. There are insufficient data available at this point to determine who is at higher risk for complications of novel influenza A (H1N1) virus infection. However, it's reasonable to assume that the same age and risk groups who are at higher risk for

seasonal influenza complications also should be considered at higher risk for novel influenza A (H1N1) complications.

Evidence that influenza can be more severe in pregnant women comes from observations during previous pandemics and from studies among pregnant women who had seasonal influenza. An excess of influenza-associated excess deaths among pregnant women were reported during the pandemics of 1918–1919 and 1957–1958. Adverse pregnancy outcomes have been reported following previous influenza pandemics, with increased rates of spontaneous abortion and preterm birth reported, especially among women with pneumonia. Case reports and several epidemiologic studies conducted during interpandemic periods also indicate that pregnancy increases the risk for influenza complications for the mother and might increase the risk for adverse perinatal outcomes or delivery complications.

Clinical presentation

Pregnant women with novel influenza A (H1N1) virus would be expected to present with typical acute respiratory illness (e.g., cough, sore throat, rhinorrhea) and fever or feverishness. Many pregnant women will go on to have a typical course of uncomplicated influenza. However, for some pregnant women, illness might progress rapidly, and might be complicated by secondary bacterial infections including pneumonia. Fetal distress associated with severe maternal illness can occur. Pregnant women who have suspected novel influenza A (H1N1) virus infection should be tested, and specimens from women who have unsubtypeable influenza A virus infections should have [specimens](#) sent to the state public health laboratory for additional testing to identify novel influenza A (H1N1).

Treatment and chemoprophylaxis

The currently circulating novel influenza A (H1N1) virus is sensitive to the neuraminidase inhibitor antiviral medications zanamivir (Relenza[®]) and oseltamivir (Tamiflu[®]), but is resistant to the adamantane antiviral medications, amantadine (Symmetrel[®]) and rimantadine (Flumadine[®]). Pregnant women who meet current [case-definitions](#) for confirmed, probable or suspected novel influenza A (H1N1) infection should receive empiric antiviral treatment. Pregnant women who are close contacts with persons with suspected, probable or confirmed cases of novel influenza A (H1N1) should receive chemoprophylaxis.

As is recommended for other persons who are treated, antiviral treatment with zanamivir or oseltamivir should be initiated as soon as possible after the onset of influenza symptoms, with benefits expected to be greatest if started within 48 hours of onset, based on data from studies of seasonal influenza. However, some data from studies on seasonal influenza indicate benefit for hospitalized patients even if treatment is started more than 48 hours after onset. Recommended duration of treatment is five days, and for chemoprophylaxis is 10 days. Oseltamivir and zanamivir treatment and chemoprophylaxis regimens recommended for pregnant women are the same as those recommended for adults who have seasonal influenza. [Recommendations](#) for use of antivirals for pregnant women might change as data on antiviral susceptibilities become available.

One of the more well-studied adverse effects of influenza is its associated hyperthermia. Studies have shown that maternal hyperthermia during the first trimester doubles the risk of neural tube defects and may be associated with other birth defects and adverse outcomes. Limited data suggest that the risk for birth defects associated with fever might be mitigated by antipyretic medications or multivitamins that contain folic acid. Maternal fever during labor has been shown to be a risk factor for adverse neonatal and developmental outcomes, including neonatal seizures, encephalopathy, cerebral palsy, and neonatal death. Even though distinguishing the

effects of the cause of fever from the hyperthermia itself is difficult, fever in pregnant women should be treated because of the risk that hyperthermia appears to pose to the fetus. Acetaminophen appears to be the best option for treatment of fever during pregnancy, although data on even this common exposure are also limited.

Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use. Pregnant women might be at higher risk for severe complications from novel influenza A (H1N1), and the benefits of treatment or chemoprophylaxis with zanamivir or oseltamivir likely outweigh the theoretical risks of antiviral use. Oseltamivir and zanamivir are "Pregnancy Category C" medications, indicating that no clinical studies have been conducted to assess the safety of these medications for pregnant women. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, oseltamivir or zanamivir should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus. Although a few adverse effects have been reported in pregnant women who took these medications, no relation between the use of these medications and those adverse events has been established. Because of its systemic activity, oseltamivir is preferred for treatment of pregnant women. The drug of choice for prophylaxis is less clear. Zanamivir may be preferable because of its limited systemic absorption; however, respiratory complications that may be associated with zanamivir because of its inhaled route of administration need to be considered, especially in women at risk for respiratory problems.

Table 1. Antiviral medication dosing recommendations for treatment or chemoprophylaxis of novel influenza A (H1N1) infection. (Table extracted from IDSA guidelines for seasonal influenza)			
Agent, Group		Treatment	Chemoprophylaxis
Oseltamivir (Tamiflu)			
Adults		75-mg capsule twice per day for 5 days	75-mg capsule once per day
Children ≥ 12 months	15 kg or less	60 mg per day divided into 2 doses	30 mg once per day
	15-23 kg	90 mg per day divided into 2 doses	45 mg once per day
	24-40 kg	120 mg per day divided into 2 doses	60 mg once per day
	>40 kg	150 mg per day divided into 2 doses	75 mg once per day
Zanamivir			
Adults		Two 5-mg inhalations (10 mg total) twice per day	Two 5-mg inhalations (10 mg total) once per day
Children		Two 5-mg inhalations (10 mg total) twice per day (age, 7 years or older)	Two 5-mg inhalations (10 mg total) once per day (age, 5 years or older)

Other ways to reduce risk for pregnant women


There is no vaccine available yet to prevent novel influenza A (H1N1); however, the risk for novel influenza A (H1N1) might be reduced by taking steps to reduce the chance of being exposed to respiratory infections. These actions include frequent hand washing, covering coughs, and having ill persons stay home except to seek medical care, and minimize contact with others in the household. Additional measures that can limit transmission of a new influenza strain include voluntary home quarantine of members of households with confirmed or probable novel influenza A (H1N1) cases, reduction of unnecessary social contacts, and avoidance whenever possible of crowded settings. If used correctly, facemasks and respirators may help reduce the risk of getting influenza, but they should be used along with other preventive measures, such as avoiding close contact and maintaining good hand hygiene. A respirator that fits snugly on the face can filter out

small particles that can be inhaled around the edges of a facemask, but compared with a facemask it is harder to breathe through a respirator for long periods of time.

Breastfeeding considerations

Infants who are not breastfeeding are particularly vulnerable to infection and hospitalization for severe respiratory illness. Women who deliver should be encouraged to initiate breastfeeding early and feed frequently. Ideally, babies should receive most of their nutrition from breast milk. Eliminate unnecessary formula supplementation, so the infant can receive as much maternal antibodies as possible.

If a woman is ill, she should continue breastfeeding and increase feeding frequency. If maternal illness prevents safe feeding at the breast, but she can still pump, encourage her to do so. The risk for novel influenza A (H1N1) transmission through breast milk is unknown. However, reports of viremia with seasonal influenza infection are rare.

Expressed milk should be used for infants too ill to feed at the breast. In certain situations, infants may be able to use donor human milk from a [HMBANA-certified milk bank](#).

Antiviral medication treatment or prophylaxis is not a contraindication for breastfeeding.

Instruct parent and caretakers on how to protect their infant from the spread of germs that cause respiratory illnesses like novel influenza A (H1N1):

- Wash adults' and infants' hands frequently with soap and water, especially after infants place their hands in their mouths.
- Keep infants and mothers as close together as possible and encourage early and frequent skin-to-skin contact between mothers and their infants.
- Limit sharing of toys and other items that have been in infants' mouths. Wash thoroughly with soap and water any items that have been in infants' mouths.
- Keep pacifiers (including the pacifier ring/handle) and other items out of adults' or other infants' mouths prior to giving to the infant.
- Practice cough and sneeze etiquette.

Citation

Centers for Disease Control and Prevention (CDC). Novel influenza A (H1N1) virus infections in three pregnant women — United States, April–May 2009. *MMWR Morb Mortal Wkly Rep* 2009 May 15; 58:497. (URL: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0512a1.htm>).