



Novel Influenza A (H1N1) Virus Infections in Three Pregnant Women – United States, April–May 2009

CDC first identified cases of respiratory infection with a novel influenza A (H1N1) virus in the United States on April 15 and 17, 2009 (1). During seasonal influenza epidemics and previous pandemics, pregnant women have been at increased risk for complications related to influenza infection (2–5). In addition, maternal influenza virus infection and accompanying hyperthermia place fetuses at risk for complications such as birth defects and preterm birth (6). As part of surveillance for infection with the novel influenza A (H1N1) virus, CDC initiated surveillance for pregnant women who were infected with the novel virus. As of May 10, a total of 20 cases of novel influenza A (H1N1) virus infection had been reported among pregnant women in the United States, including 15 confirmed cases and five probable cases.* Among the 13 women from seven states for whom data are available, the median age was 26 years (range: 15–39 years); three women were hospitalized, one of whom died. This report provides preliminary details of three cases of novel influenza A (H1N1) virus infection in pregnant women. Pregnant women with confirmed, probable, or suspected novel influenza A (H1N1) virus infection should receive antiviral treatment for 5 days. Oseltamivir is the preferred treatment for pregnant women, and the drug regimen should be initiated within 48 hours of symptom onset, if possible. Pregnant women who are in close contact with a person with confirmed, probable, or suspected novel influenza A (H1N1) infection should receive a 10-day course of chemoprophylaxis with zanamivir or oseltamivir.

Case Reports

Patient A. On April 15, a woman aged 33 years at 35 weeks' gestation with a 1-day history of myalgias, dry cough, and low-grade fever was examined by her obstetrician-gynecologist. She had been in relatively good health and had been taking no medications other than prenatal vitamins, although she had a history of psoriasis and mild asthma. The patient had not

recently traveled to Mexico. Rapid influenza diagnostic testing performed in the physician's office was positive.

On April 19, she was examined in a local emergency department, with worsening shortness of breath, fever, and productive cough. She experienced severe respiratory distress, with an oxygen saturation of approximately 80% on room air and a respiratory rate of approximately 30 breaths per minute. A chest radiograph revealed bilateral nodular infiltrates. The patient required intubation and was placed on mechanical ventilation. On April 19, an emergency cesarean delivery was performed, resulting in a female infant with Apgar scores of 4 at 1 minute after birth and of 6 at 5 minutes after birth; the infant is healthy and has been discharged home. On April 21, the patient developed acute respiratory distress syndrome (ARDS). The patient began receiving oseltamivir on April 28. She also received broad-spectrum antibiotics and remained on mechanical ventilation. The patient died on May 4.

On April 25, a nasopharyngeal swab specimen collected from patient A indicated an unsubtypeable influenza A strain by real-time reverse transcription–polymerase chain reaction (rRT-PCR) at the San Antonio Metro Health Laboratory. The specimen was forwarded to the Virus Surveillance and Diagnostic Branch Laboratory, Influenza Division, CDC, where testing was inconclusive for novel influenza A (H1N1) virus. On April 30, a repeat nasopharyngeal specimen was collected, which was positive by rRT-PCR for novel influenza A (H1N1) virus at CDC.

Patient B. A previously healthy woman aged 35 years at 32 weeks' gestation was seen at a local emergency department on April 20 with a 1-day history of shortness of breath, fever, cough, diarrhea, headache, myalgias, sore throat, and inspiratory chest pain. She was febrile (101.6°F [38.7°C]), with a heart rate of 128 beats per minute, respiratory rate of 22 breaths per minute, and oxygen saturation of >97% on room air. A chest radiograph was normal. Rapid influenza diagnostic testing was negative. The patient received a parenteral nonsteroidal anti-inflammatory medication, acetaminophen, and inhaled albuterol and was discharged home. She was evaluated the

* Case definitions available at <http://www.cdc.gov/h1n1flu/casedef.htm>.

following day in her obstetrician-gynecologist's office, where a nasopharyngeal swab sample was collected and sent for rRT-PCR testing. The patient received antibiotics, anti-nausea medication, acetaminophen, and an inhaled corticosteroid. The patient recovered fully, and her pregnancy is proceeding normally.

Patient B had been in Mexico during the 3 days preceding her arrival at the emergency department. Several family members in Mexico and the United States had recently been ill with influenza-like illness, and her sister had been hospitalized for pneumonia during the preceding week. Testing of the nasopharyngeal swab specimen from patient B collected on April 21 was identified as an unsubtypable influenza A strain by rRT-PCR testing at the Naval Health Research Laboratory in San Diego. Additional testing at CDC confirmed infection with novel influenza A (H1N1) virus.

Patient C. On April 29, a woman aged 29 years at 23 weeks' gestation was experiencing cough, sore throat, chills, subjective fever, and weakness of 1 day's duration and was seen at the family practice clinic where she had been receiving prenatal care. The patient had a history of asthma but was not taking any asthma medications. Her son, aged 10 years, reportedly had similar symptoms the week before the onset of her symptoms. Another son, aged 7 years, had become ill on the same day as his mother and accompanied her to the clinic. At the clinic, the younger son was coughing vigorously and was asked to put on a mask by office staff members. Rapid influenza diagnostic testing in the family practice clinic of a nasopharyngeal sample from patient C was positive. The woman was prescribed oseltamivir, which she began taking later the same day. Her symptoms are resolving without complications, and her pregnancy is proceeding normally.

Patient C had not traveled to Mexico recently. Her son aged 7 years also was prescribed oseltamivir on April 29 but was not tested for influenza. The physician who evaluated patient C was also pregnant (13 weeks' gestation). The physician began chemoprophylaxis with oseltamivir and has remained asymptomatic.

A nasopharyngeal swab collected from patient C on April 29 was identified as an unsubtypable influenza A strain by the Washington State Public Health Laboratory. Additional testing at CDC confirmed infection with novel influenza A (H1N1) virus.

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Editorial Note: This report provides preliminary details on three cases of novel influenza A (H1N1) virus infection in pregnant women. Additional information on these cases and other pregnant women with this infection is being compiled by CDC based on reports from state health departments. The three pregnant women described in this report all initially had symptoms of acute febrile respiratory illness similar to the clinical symptoms in nonpregnant women with the infection; one patient (patient A) developed ARDS and died. The most frequently reported symptoms among nonpregnant patients with novel influenza A (H1N1) virus infection have been fever, cough, and sore throat (1).

Although data are insufficient to determine who is at highest risk for complications of novel influenza A (H1N1) virus infection, seasonal influenza epidemics (2,3) and previous influenza pandemics (4,5) have shown that pregnant women generally are at higher risk for influenza-associated morbidity and mortality compared with women who are not pregnant. The increased risk of complications is thought to be related to several physiologic changes that occur during pregnancy, including alterations in the cardiovascular, respiratory, and immune systems (7). Pregnant women with underlying medical conditions such as asthma are at particularly high risk for influenza-related complications (2). Because pregnant women are at increased risk for influenza complications, the Advisory Committee on Immunization Practices and the American College of Obstetricians and Gynecologists have recommended that women receive the trivalent inactivated influenza vaccine (8).

The novel influenza A (H1N1) virus that is circulating is susceptible to the neuraminidase inhibitor antiviral medications, oseltamivir and zanamivir (1). In randomized, placebo-controlled trials among outpatients, these medications have reduced the severity and duration of symptoms of seasonal influenza if started within 48 hours of illness onset, and limited data from observational studies among hospitalized patients with seasonal influenza indicate that oseltamivir can reduce mortality, even when started >48 hours after illness onset (8). In addition, oseltamivir and zanamivir have been highly effective in preventing seasonal influenza if used shortly after exposure to the disease (8). Little information is available on the safety or effectiveness of these medications when used during pregnancy (9,10). However, considering the limited

information available and the known risks for influenza complications during pregnancy, any potential risk to a fetus likely is outweighed by the expected benefits of influenza antiviral treatment for this novel virus. Thus, CDC interim guidance indicates that pregnant women with confirmed, probable, or suspected novel influenza A (H1N1) virus infection should receive antiviral treatment for 5 days.[†]

Although zanamivir can be used in pregnancy, oseltamivir is preferred for treatment of pregnant women because of its systemic absorption (10). Theoretically, higher systemic absorption might suppress influenza viral loads more effectively in sites other than the respiratory system (e.g., placenta) and might provide better protection against mother-child transmission. Similar to the recommendation for nonpregnant persons who are treated, oseltamivir treatment should be initiated as soon as possible, ideally within 48 hours of onset of symptoms. In addition, any pregnant woman hospitalized with confirmed, probable, or suspected novel influenza A (H1N1) virus infection should receive oseltamivir, even if >48 hours have elapsed since illness onset (8). Beginning treatment as early as possible is critical. In addition, treating fevers in pregnant women with acetaminophen is important because maternal hyperthermia has been associated with various adverse fetal and neonatal outcomes (6).

In all clinical settings, including settings that provide care for pregnant women, patients should be screened for signs and symptoms of febrile respiratory illness at the initial point of contact, and these patients should be promptly segregated and assessed. Outpatient clinical settings and labor and delivery units should develop and implement procedures for handling patients with respiratory illness and friends or family members who might accompany them. Pregnant women who are in close contact with a person who has a confirmed, probable, or suspected case should receive a 10-day course of chemoprophylaxis with zanamivir or oseltamivir. For chemoprophylaxis in pregnant patients, a preferred anti-influenza medication has not been determined. Although zanamivir might have the benefit of more limited systemic absorption (9), respiratory symptoms such as coughing or severe nasal congestion might limit its

usefulness because of its inhaled route of administration. The pregnant physician caring for patient C began chemoprophylaxis soon after exposure.

Because of the increased risk for severe complications, the public health response to outbreaks of novel influenza A (H1N1) virus should include considerations specific to pregnant women. Interim guidance on issues specific to pregnant women and the novel influenza A (H1N1) virus is available at http://www.cdc.gov/h1n1flu/clinician_pregnant.htm. Additional information regarding novel influenza A (H1N1) virus is available at <http://www.cdc.gov/h1n1flu>. Clinicians should report cases of novel influenza A (H1N1) virus infection in pregnant women to their state or local health departments or CDC.

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References

1. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med* 2009;361. [E-pub ahead of print].
2. Dodds L, McNeil SA, Fell DB, et al. Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. *CMAJ* 2007;176:463–8.
3. Neuzil KM, Reed GW, Mitchel EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol* 1998;148:1094–102.
4. Freeman DW, Barno A. Deaths from Asian influenza associated with pregnancy. *Am J Obstet Gynecol* 1959;78:1172–5.
5. Harris JW. Influenza occurring in pregnant women. *JAMA* 1919;72:978–80.
6. Rasmussen SA, Jamieson DJ, Bresee JS. Pandemic influenza and pregnant women. *Emerg Infect Dis* 2008;14:95–100.
7. Jamieson DJ, Theiler RN, Rasmussen SA. Emerging infections and pregnancy. *Emerg Infect Dis* 2006;12:1638–43.
8. CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008. *MMWR* 2008;57(No. RR-7).
9. Freund B, Gravenstein S, Elliott M, Miller I. Zanamivir: a review of clinical safety. *Drug Saf* 1999;21:267–81.
10. Ward P, Small I, Smith J, Suter P, Dutkowski R. Oseltamivir (Tamiflu) and its potential for use in the event of an influenza pandemic. *J Antimicrob Chemother* 2005;55(Suppl 1):i5–21.

[†] Guidance available at http://www.cdc.gov/h1n1flu/clinician_pregnant.htm.