



Swine Influenza A (H1N1) Infection in Two Children – Southern California, March–April 2009

On April 17, 2009, CDC determined that two cases of febrile respiratory illness occurring in children who resided in adjacent counties in southern California were caused by infection with a swine influenza A (H1N1) virus. The viruses from the two cases are closely related genetically, resistant to amantadine and rimantadine, and contain a unique combination of gene segments that previously has not been reported among swine or human influenza viruses in the United States or elsewhere. Neither child had contact with pigs; the source of the infection is unknown. Investigations to identify the source of infection and to determine whether additional persons have been ill from infection with similar swine influenza viruses are ongoing. This report briefly describes the two cases and the investigations currently under way. Although this is not a new subtype of influenza A in humans, concern exists that this new strain of swine influenza A (H1N1) is substantially different from human influenza A (H1N1) viruses, that a large proportion of the population might be susceptible to infection, and that the seasonal influenza vaccine H1N1 strain might not provide protection. The lack of known exposure to pigs in the two cases increases the possibility that human-to-human transmission of this new influenza virus has occurred. Clinicians should consider animal as well as seasonal influenza virus infections in their differential diagnosis of patients who have febrile respiratory illness and who 1) live in San Diego and Imperial counties or 2) traveled to these counties or were in contact with ill persons from these counties in the 7 days preceding their illness onset, or 3) had recent exposure to pigs. Clinicians who suspect swine influenza virus infections in a patient should obtain a respiratory specimen and contact their state or local health department to facilitate testing at a state public health laboratory.

Case Reports

Patient A. On April 13, 2009, CDC was notified of a case of respiratory illness in a boy aged 10 years who lives in San Diego County, California. The patient had onset of fever, cough, and vomiting on March 30, 2009. He was taken to an

outpatient clinic, and a nasopharyngeal swab was collected for testing as part of a clinical study. The boy received symptomatic treatment, and all his symptoms resolved uneventfully within approximately 1 week. The child had not received influenza vaccine during this influenza season. Initial testing at the clinic using an investigational diagnostic device identified an influenza A virus, but the test was negative for human influenza subtypes H1N1, H3N2, and H5N1. The San Diego County Health Department was notified, and per protocol, the specimen was sent for further confirmatory testing to reference laboratories, where the sample was verified to be an unsubtypable influenza A strain. On April 14, 2009, CDC received clinical specimens and determined that the virus was swine influenza A (H1N1). The boy and his family reported that the child had had no exposure to pigs. Investigation of potential animal exposures among the boy's contacts is continuing. The patient's mother had respiratory symptoms without fever in the first few days of April 2009, and a brother aged 8 years had a respiratory illness 2 weeks before illness onset in the patient and had a second illness with cough, fever, and rhinorrhea on April 11, 2009. However, no respiratory specimens were collected from either the mother or brother during their acute illnesses. Public health officials are conducting case and contact investigations to determine whether illness has occurred among other relatives and contacts in California, and during the family's travel to Texas on April 3, 2009.

Patient B. CDC received an influenza specimen on April 17, 2009, that had been forwarded as an unsubtypable influenza A virus from the Naval Health Research Center in San Diego, California. CDC identified this specimen as a swine influenza A (H1N1) virus on April 17, 2009, and notified the California Department of Public Health. The source of the specimen, patient B, is a girl aged 9 years who resides in Imperial County, California, adjacent to San Diego County. On March 28, 2009, she had onset of cough and fever (104.3°F [40.2°C]). She was taken to an outpatient facility that was participating in an influenza surveillance project, treated with amoxicillin/

clavulanate potassium and an antihistamine, and has since recovered uneventfully. The child had not received influenza vaccine during this influenza season. The patient and her parents reported no exposure to pigs, although the girl did attend an agricultural fair where pigs were exhibited approximately 4 weeks before illness onset. She reported that she did not see pigs at the fair and went only to the amusement section of the fair. The Imperial County Public Health Department and the California Department of Public Health are now conducting an investigation to determine possible sources of infection and to identify any additional human cases. The patient's brother aged 13 years had influenza-like symptoms on April 1, 2009, and a male cousin aged 13 years living in the home had influenza-like symptoms on March 25, 2009, 3 days before onset of the patient's symptoms. The brother and cousin were not tested for influenza at the time of their illnesses.

Epidemiologic and Laboratory Investigations

As of April 21, 2009, no epidemiologic link between patients A and B had been identified, and no additional cases of infection with the identified strain of swine influenza A (H1N1) had been identified. Surveillance data from Imperial and San Diego counties, and from California overall, showed declining influenza activity at the time of the two patients' illnesses. Case and contact investigations by the county and state departments of health in California and Texas are ongoing. Enhanced surveillance for possible additional cases is being implemented in the area.

Preliminary genetic characterization of the influenza viruses has identified them as swine influenza A (H1N1) viruses. The viruses are similar to each other, and the majority of their genes, including the hemagglutinin (HA) gene, are similar to those of swine influenza viruses that have circulated among U.S. pigs since approximately 1999; however, two genes coding for the neuraminidase (NA) and matrix (M) proteins are similar to corresponding genes of swine influenza viruses of the Eurasian lineage (1). This particular genetic combination of swine influenza virus segments has not been recognized previously among swine or human isolates in the United States, or elsewhere based on analyses of influenza genomic sequences available on GenBank.* Viruses with this combination of genes are not known to be circulating among swine in the United States; however, no formal national surveillance system exists to determine what viruses are prevalent in the U.S. swine population. Recent collaboration between the U.S. Department of Agriculture and CDC has led to development of a pilot swine

influenza virus surveillance program to better understand the epidemiology and ecology of swine influenza virus infections in swine and humans.

The viruses in these two patients demonstrate antiviral resistance to amantadine and rimantadine, and testing to determine susceptibility to the neuraminidase inhibitor drugs oseltamivir and zanamivir is under way. Because these viruses carry a unique combination of genes, no information currently is available regarding the efficiency of transmission in swine or in humans. Investigations to understand transmission of this virus are ongoing.

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Editorial Note: In the past, CDC has received reports of approximately one human swine influenza virus infection every 1–2 years in the United States (2,3). However, during December 2005–January 2009, 12 cases of human infection with swine influenza were reported; five of these 12 cases occurred in patients who had direct exposure to pigs, six in patients reported being near pigs, and the exposure in one case was unknown (1,4,5). In the United States, novel influenza A virus infections in humans, including swine influenza infections, have been nationally notifiable conditions since 2007. The recent increased reporting might be, in part, a result of increased influenza testing capabilities in public health laboratories, but genetic changes in swine influenza viruses and other factors also might be a factor (1,4,5). Although the vast majority of human infections with animal influenza viruses do not result in human-to-human transmission (2,3), each case should be fully investigated to be certain that such viruses are not spreading among humans and to limit further exposure of humans to infected animals, if infected animals are identified. Such investigations should include close collaboration between state and local public health officials with animal health officials.

* Available at <http://www.ncbi.nlm.nih.gov/Genbank>.

The lack of known exposure to pigs in the two cases described in this report increases the possibility that human-to-human transmission of this new influenza virus has occurred. Clinicians should consider animal as well as seasonal influenza virus infections in the differential diagnosis of patients with febrile respiratory illness who live in San Diego and Imperial counties or have traveled to these areas or been in contact with ill persons from these areas in the 7 days before their illness onset. In addition, clinicians should consider animal influenza infections among persons with febrile respiratory illness who have been near pigs, such as attending fairs or other places where pigs might be displayed. Clinicians who suspect swine influenza virus infections in humans should obtain a nasopharyngeal swab from the patient, place the swab in a viral transport medium, and contact their state or local health department to facilitate transport and timely diagnosis at a state public health laboratory. CDC requests that state public health laboratories send all influenza A specimens that cannot be subtyped to the CDC, Influenza Division, Virus Surveillance and Diagnostics Branch Laboratory.

Interim guidance on infection control, treatment, and chemoprophylaxis for swine influenza is available at <http://www.cdc.gov/flu/swine/recommendations.htm>. Additional information about swine influenza is available at <http://www.cdc.gov/flu/swine/index.htm>.

References

1. Vincent AL, Ma W, Lager KM, Janke BH, Richt JA. Swine influenza viruses: a North American perspective. *Adv Virus Res* 2008;72:127–54.
2. Myers KP, Olsen CW, Gray GC. Cases of swine influenza in humans: a review of the literature. *Clin Infect Dis* 2007;44:1084–8.
3. Wells DL, Hopfensperger DJ, Arden NH, et al. Swine influenza virus infections. Transmission from ill pigs to humans at a Wisconsin agricultural fair and subsequent probable person-to-person transmission. *JAMA* 1991;265:478–81.
4. Vincent AL, Swenson SL, Lager KM, Gauger PC, Loiacono C, Zhang Y. Characterization of an influenza A virus isolated from pigs during an outbreak of respiratory disease in swine and people during a county fair in the United States. *Vet Microbiol* 2009;online publication ahead of print.
5. Newman AP, Reisdorf E, Beinemann J, et al. Human case of swine influenza A (H1N1) triple reassortant virus infection, Wisconsin. *Emerg Infect Dis* 2008;14:1470–2.