

Swine-Origin Influenza A (H3N2) Virus Infection in Two Children — Indiana and Pennsylvania, July–August 2011

Influenza A viruses are endemic in many animal species, including humans, swine, and wild birds, and sporadic cases of transmission of influenza A viruses between humans and animals do occur, including human infections with avian-origin influenza A viruses (i.e., H5N1 and H7N7) and swine-origin influenza A viruses (i.e., H1N1, H1N2, and H3N2) (1). Genetic analysis can distinguish animal origin influenza viruses from the seasonal human influenza viruses that circulate widely and cause annual epidemics. This report describes two cases of febrile respiratory illness caused by swine-origin influenza A (H3N2) viruses identified on August 19 and August 26, 2011, and the current investigations. No epidemiologic link between the two cases has been identified, and although investigations are ongoing, no additional confirmed human infections with this virus have been detected. These viruses are similar to eight other swine-origin influenza A (H3N2) viruses identified from previous human infections over the past 2 years, but are unique in that one of the eight gene segments (matrix [M] gene) is from the 2009 influenza A (H1N1) virus. The acquisition of the M gene in these two swine-origin influenza A (H3N2) viruses indicates that they are “reassortants” because they contain genes of the swine-origin influenza A (H3N2) virus circulating in North American pigs since 1998 (2) and the 2009 influenza A (H1N1) virus that might have been transmitted to pigs from humans during the 2009 H1N1 pandemic. However, reassortments of the 2009 influenza A (H1N1) virus with other swine influenza A viruses have been reported previously in swine (3). Clinicians who suspect influenza virus infection in humans with recent exposure to swine should obtain a nasopharyngeal swab from the patient for timely diagnosis at a state public health laboratory and consider empiric neuraminidase inhibitor antiviral treatment to quickly limit potential human transmission (4).

Case Reports

Patient A. On August 17, 2011, CDC was notified by the Indiana State Department of Health Laboratories of a suspected case of swine-origin influenza A (H3N2) infection in a boy aged <5 years. The boy, who had received influenza vaccine in September 2010, experienced onset of fever, cough, shortness of breath, diarrhea, and sore throat on July 23, 2011. He was brought to a local emergency department (ED) where a respiratory specimen later tested positive for influenza A (H3). The boy was discharged home, but was not treated with influenza antiviral medications. He has multiple chronic health conditions, returned to the ED on July 24, 2011, and was hospitalized for treatment of those health problems, which had worsened. The boy was discharged home on July 27, 2011, and has since recovered from this illness. As part of routine CDC-supported influenza surveillance, the respiratory specimen collected on July 24, 2011, was forwarded to the Indiana State Department of Health Laboratories, where polymerase chain reaction (PCR) testing identified a suspect swine-origin influenza A (H3N2) virus on August 17, 2011. The specimen was forwarded to CDC where the findings were confirmed through genome sequencing on August 19, 2011.

No direct exposure to swine was identified for this child; however, a caretaker reported direct contact with asymptomatic swine in the weeks before the boy's illness onset and provided care to the child 2 days before illness onset. No respiratory illness was identified in any of the child's family or close contacts, the boy's caretaker, or in the family or contacts of the caretaker.

Patient B. On August 24, 2011, CDC was notified by the Pennsylvania Department of Health of a suspected case of swine-origin influenza A (H3N2) virus infection in a girl aged <5 years. The girl, who had received influenza



vaccine in September 2010, experienced acute onset of fever, nonproductive cough, and lethargy on August 20, 2011. She was brought to a local hospital ED where a nasopharyngeal swab tested positive for influenza A by rapid influenza diagnostic test. She was not treated with influenza antiviral medications and was discharged home the same day. The girl has completely recovered from this illness.

A nasopharyngeal swab and nasal wash specimen were obtained at the ED and forwarded to the Pennsylvania State Department of Health Bureau of Laboratories for additional testing as part of routine CDC-supported influenza surveillance. On August 23, 2011, the state public health laboratory identified a suspected swine-origin influenza A (H3N2) virus by PCR testing, and both specimens were forwarded to CDC. On August 26, 2011, genome sequencing confirmed the virus as swine-origin influenza A (H3N2). On August 16, 2011, the girl was reported to have visited an agricultural fair where she had direct exposure to swine and other animals. No additional illness in the girl's family or close contacts has been identified, but illness in other fair attendees continues to be investigated. No additional confirmed swine-origin influenza virus infections have been identified thus far.

Epidemiologic and Laboratory Investigations

As of September 2, 2011, no epidemiologic link between patients A and B had been identified, and no additional cases of confirmed infection with the identified strain of swine-origin influenza A (H3N2) virus had been identified. Surveillance data from both states showed low levels of influenza activity at the time of both patients' illnesses. Case and contact investigations by the county and state human and animal health agencies in Indiana and Pennsylvania are ongoing, and enhanced surveillance for additional human cases is being implemented in both states.

Preliminary genetic characterization of these two influenza viruses has identified them as swine-origin influenza A (H3N2) viruses. Full genome sequences have been posted to publicly available web sites. The viruses are similar, but not identical to each other. Seven of the eight gene segments, including the hemagglutinin (HA) and neuraminidase (NA) genes, are similar to those of swine H3N2 influenza viruses circulating among U.S. pigs since 1998 (2) and previously identified in the eight other sporadic cases of human infection with swine-origin influenza A (H3N2) viruses in the United States since 2009.* The one notable difference from the viruses previously identified in human infections with swine-origin influenza A (H3N2) virus is that these two viruses have a matrix (M) gene

acquired from the 2009 influenza A (H1N1) virus, replacing the classical swine M gene present in the prior eight swine-origin influenza A (H3N2) virus infections in humans.

Although reassortment between swine influenza and 2009 influenza A (H1N1) viruses has been reported in pigs in the United States (3), this particular genetic combination of swine influenza virus segments is unique and has not been reported previously in either swine or humans, based on a review of influenza genomic sequences publicly available in GenBank.† Analysis of data submitted to GenBank via the U.S. Department of Agriculture (USDA) Swine Influenza Virus Surveillance Program subsequent to this case identified two additional influenza A (H3N2) isolates from swine containing the M gene from the 2009 influenza A (H1N1) virus. Genome sequencing is underway to completely characterize the genetic composition of these two swine influenza isolates. (USDA Agricultural Research Service and USDA Animal and Plant Health Inspection Service, unpublished data, 2011).

The viruses in these two patients are resistant to amantadine and rimantadine, but are susceptible to the neuraminidase inhibitor drugs oseltamivir and zanamivir. Because these viruses carry a unique combination of genes, no information currently is available regarding the capacity of this virus to transmit efficiently in swine, humans, or between swine and humans.

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

*Additional information is available at <http://www.cdc.gov/flu/weekly/pastreports.htm>.

What is already known on this topic?

During December 2005–November 2010, 21 cases of human infection with swine-origin influenza were reported, including 12 cases with swine-origin influenza A (H1N1) virus infection, eight cases with swine-origin influenza A (H3N2) virus infection, and one case with swine-origin influenza A (H1N2) virus infection.

What is added by this report?

This report describes two cases of febrile respiratory illness caused by swine-origin influenza A (H3N2) viruses identified on August 19 and August 26, 2011. The viruses identified in these cases are unique in that one of the eight gene segments (matrix [M] gene) is from the 2009 influenza A (H1N1) virus.

What are the implications for public health practice?

Non-human influenza virus infections rarely result in human-to-human transmission, but the implications of sustained ongoing transmission between humans is potentially severe; therefore, prompt and thorough identification and investigation of these sporadic human infections with non-human influenza viruses are needed to reduce the risk for sustained transmission.

Editorial Note

To detect human infections with animal influenza viruses more effectively, CDC and state and local health departments have strengthened laboratory and epidemiologic procedures to promptly detect sporadic cases such as these. Since 2005, state public health laboratories have had the capability to detect non-human origin–influenza A viruses by PCR testing. From 2005 to 2007, CDC received reports of approximately one human infection with a swine-origin influenza virus each year. In 2007, human infection with a novel influenza A virus, including swine-origin influenza virus infections, became a nationally notifiable condition. Since that time, CDC has received approximately three to five reports a year of human infections with swine-origin influenza viruses. The recent increase in reporting might be, in part, a result of increased influenza testing capabilities in public health laboratories that allows for identification of human and swine-origin influenza viruses, but genetic changes in swine influenza viruses and other factors also might be contributing to this increase (5–7). During December 2005–November 2010, before the two cases described in this report, 21 cases of human infection with swine-origin influenza were reported (12 cases with swine-origin influenza A (H1N1) virus infection, eight cases with swine-origin influenza A (H3N2) virus infection, and one case

with swine-origin influenza A (H1N2) virus infection). Six of these 21 cases occurred in patients who reported direct exposure to pigs; 12 patients reported being near pigs; human-to-human transmission was suspected in two cases after epidemiologic investigations revealed no reported contact with swine in either case, but contact with ill persons who reported swine exposure was the suspected source of infection; the exposure in one case was unknown (8) (CDC, unpublished data; 2011). Although the vast majority of human infections with animal influenza viruses do not result in human-to-human transmission (9,10), each case should be investigated fully to ascertain whether these viruses are transmitted among humans and to limit further exposure of humans to infected animals, if infected animals are identified. Such investigations require close collaboration between CDC, state and local public health officials, and animal health officials.

The lack of known direct exposure to pigs in one of the two cases described in this report suggests the possibility that limited human-to-human transmission of this influenza virus occurred. Likely transmission of swine-origin influenza A (H3N2) virus from close contact with an infected person has been observed in past investigations of human infections with swine-origin influenza A virus, but has not resulted in sustained human-to-human transmission. Preliminary evidence from the investigation of the Indiana case shows no ongoing transmission. No influenza illness has been identified, but if additional chains of transmission are identified rapid intervention is warranted try to prevent further spread of the virus. Clinicians should consider swine-origin influenza A virus infection as well as seasonal influenza virus infections in the differential diagnosis of patients with febrile respiratory illness who have been near pigs. Clinicians who suspect influenza virus infection in humans with recent exposure to swine, should obtain a nasopharyngeal swab from the patient, place the swab in a viral transport medium, contact their state or local health department to facilitate transport and timely diagnosis at a state public health laboratory, and consider empiric neuraminidase inhibitor antiviral treatment (4). CDC requests that state public health laboratories send all suspected swine-origin influenza A specimens to the CDC, Influenza Division, Virus Surveillance and Diagnostics Branch Laboratory.

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