



ECDC Threat Assessment - UPDATE

Human cases of swine influenza without apparent exposure to pigs,

United States and Mexico

24 April 2009 – 19:00 hours

SOURCE AND DATE OF REQUEST

ECDC internal decision, 22 April 2009

PUBLIC HEALTH ISSUE

Implication for Europe of the identification of human cases of swine influenza A, with a unique gene segment combination

DISEASE BACKGROUND INFORMATION

Human infection and disease

Infection with swine influenza virus has been detected occasionally in humans since the 1950s and human disease is usually clinically similar to disease caused by infections with human influenza viruses [4-9]. Complications that include pneumonia and death have been reported in the literature in otherwise healthy adults without underlying disease [1].

Cases of swine influenza in humans usually occur after a history of exposure to pigs, i.e. direct or close (within 6 feet or 1.8 m) but not indirect contact [14]. Of the 12 cases reported in the US between Dec 2005 and Jan 2009, 11 had a history of exposure to pigs; for one case exposure was unknown [13]. Single generation person-to-person transmission has been reported but appears to be rare. Chains of transmission have not been observed apart from an outbreak among young adult military recruits in an unusual basic-training centre in New Jersey in 1976, causing 230 infections, 13 of whom were severe with one death during a one-month period [15].

Serological surveys undertaken in North America among persons working with pigs have shown that they quite often have evidence of prior infection with swine influenza viruses [8, 10]. Interpretation of sero-prevalence data can be difficult due to cross-reactivity (i.e. infection with a seasonal influenza virus might be misinterpreted as indicating prior swine influenza infection). There are no contemporary serological data for Europe.

Human public health importance of swine influenza

The main public health importance of swine influenza relates to the risk of “reassortment” to produce a novel virus (possibly a pandemic strain), either in the pig or in a human by co-infection with a human and a swine strain. Triple recombinant swine influenza viruses with avian, human and swine genes have been circulating in pigs in the US, and have been transmitted to humans [7,9], but like other prevalent swine viruses belong to the same HA subtype, H1 or H3, as contemporary human viruses.

EVENT 1: BACKGROUND INFORMATION - UNITED STATES

On April 21, the United States reported on the existence of 2 human cases of swine influenza A (H1N1) infection. On 23 April, through intensified surveillance efforts, a total of 7 confirmed human cases of swine influenza A (H1N1) infection, were reported. The viruses of the 2 initial cases are closely related, presenting a unique gene segment combination that has not been previously recognised in swine or human isolates in the US or elsewhere in the world (GenBank data) and both are resistant to amantadine and rimantadine, but remain sensitive to oseltamivir and zanamivir [13]. Since the possibility of human-to-human transmission of a novel influenza virus was raised by the lack of a history of contact with pigs, the event was notified to WHO under the International Health Regulations (IHR) as a potential public health emergency of international concern.

These viruses were detected in 5 residents in Southern California (3 females and 2 males) and 2 residents of a town close to San Antonio, Texas. The age of the reported cases ranges between 9 and 54 years of age. All samples of the 7 reported cases were referred to the WHO Collaborating Centre at CDC for further testing, where swine influenza A H1N1 was confirmed.

The first two cases were in a 10 year old boy and 9 year old girl, both living in California, in 2 adjacent counties, approximately 210 km apart. They initially came to light through physicians participating in virological surveillance activities. The background information to date of these two cases can be found in the MMWR of 21 April [13]. Also, currently 2 clusters of probable human-to-human transmission can be identified amongst the 7 reported cases. The first cluster occurred in the cases from Texas, in two 16 year old boys that attend the same high school and the second cluster in a father and daughter living in California.

None of the cases report any previous exposure to pigs and no epidemiological link has been established at present between the reported clusters and remaining cases. Further investigations in the US are currently ongoing in order to assess the magnitude and potential spread of the virus.

Regarding the virus, 4 gene segments have been identified in this swine influenza A (H1N1) pertaining to: North American swine influenza, North American avian influenza, human influenza and swine influenza of Euro-Asian origin. This latter gene segment was never identified in the US. In addition, it is the first time this quadruple genetic combination has been recognized in swine influenza A (H1N1) in the US and worldwide.

EVENT 2: BACKGROUND INFORMATION - MEXICO

According to the Mexican Health Authorities (http://portal.salud.gob.mx/redirector?tipo=0&n_seccion=Boletines&seccion=2009-04-23_3868.html), there are 120 confirmed cases of respiratory illness due to influenza currently being reported throughout the country. Twenty deaths have been reported (case fatality of 17%), 13 of which in the Federal District of Mexico City, 3 in Baja California, 4 San Luis Potosi and one in Oaxaca. According to local media mass vaccination campaign was launched in Mexico City. Media reports are linking the virus from this outbreak to the swine influenza human cases in the US.

ECDC THREAT ASSESSMENT FOR THE EU

Sporadic human infection with swine influenza virus has been documented in the literature; cases were mostly confined to persons with occupational exposure to pigs [11, 12].

Several elements make this latest report from Mexico and the US different from previously documented cases in humans:

1. The detection of a new and unique gene segment combination, not previously identified/detected anywhere in the world;
2. A potentially large outbreak in Mexico and seven human infections in the US have been documented and are clustered in time and in space;
3. None of the seven human cases from the US had a history of exposure to pigs, which suggest that human-to-human infection is the likely source of transmission.
4. An observed high case fatality rate is present amongst human cases in Mexico

At present, the public health situation is limited to Mexico and the US and confirmed cases in the US presented with mild symptoms. Investigations ongoing in Mexico will reveal whether the reported severe pneumonia cases are also due to this novel influenza virus. Additional investigations, both in Mexico and in the US will shed further light on whether the virus has spread further and assess the number of persons that could have been infected.

In the event of a human case in the EU infected with this particular or another swine influenza virus, human diagnostic labs would identify an unsubtypable influenza A strain, as happened in the US, and as happened in Spain end of 2008 [16, 17]. Testing for animal influenza strains by veterinary labs or the WHO Collaborating Centre for Reference and Research on Influenza in the UK could also identify the subtype H1N1 which includes this new genetic combination in the virus.

The WHO Collaborating Centre for human influenza in the UK, is not aware of the detection of such “unsubtypable” influenza A viruses in humans in Europe apart from the Spanish Case.¹

CONCLUSIONS

The reported events in Mexico and US are unusual and therefore require vigilance, including in Europe, considering the potential public health implications of swine influenza as mentioned above. While additional investigations in Mexico and the US are needed, there is currently indication of some sustained human-to-human transmission of the virus. It is too early to say whether this will lead to a larger outbreak or could represent the appearance of potential pandemic strain of influenza virus. ECDC will continue to closely monitor the situation in Mexico and the US, provide information through its website and update this threat assessment as needed. The coming days and weeks will rapidly indicate the extent of the circulation of this particular virus. ECDC has also established contact with WHO and will continue to collaborate closely with them as the situation evolves.

In order to be prepared from a European perspective, the capacity to identify this new genetic composition is crucial. Clinicians need to consider seasonal and animal influenza in their differential diagnosis and ensure the necessary lab testing accordingly, especially in persons returning from affected areas in the US and Mexico. The collaboration between human and animal diagnostic labs is essential to ensure the identification of this new influenza virus and/or new virus strains if they were to appear in Europe.

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¹ With the exception of the Spanish swine flu case in January 2009, which was confirmed to be caused by a known swine flu virus strain, and occurred after exposure to pigs.

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