ECDC THREAT ASSESSMENT

Public health issue

Implication for Europe of the identification in North America of human cases of influenza A/H1N1, with a unique gene segment combination

Update 30 April 2009, 19:00 hours CEST

Source and date of request

ECDC internal decision, 30 April 2009

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Disease background information

Influenza A/H1N1 has genetic components from swine influenza (two different types), avian influenza and human influenza viruses. This is thus a 'quadruple' recombinant virus. Triple recombinant swine influenza viruses with avian, human and swine genes have previously been circulating in pigs in the US, and have been transmitted to humans [1, 2]. There are several recent examples where influenza viruses of animal origin have been transmitted not only from the animal to humans but also from human to human – the most obvious example being the avian H5N1 influenza which has been circulating in Southeast Asia for more than a decade, and which still causes deaths in the region (even if human-to-human transmission has been very limited for this virus).

The present virus may have animal origin, but is now clearly spreading between humans. Even so, the rate of transmission does not (based on available data) seem to be extremely high. It cannot be explained why the disease seems to be more virulent in Mexico than in other parts of the world. The virus clearly has a pandemic potential, but it should be noted that the word 'pandemic' strictly just describes a disease that spreads around the world – it does not necessarily imply a severe disease.

Even if uncertain, there is suspicion that the virus originated in pigs. There have been no reports of recent influenza outbreaks in pigs in Mexico, but such infection may be asymptomatic. Infection with swine influenza virus has been detected occasionally in humans since the 1950s and human disease is usually clinically similar to

Stockholm, April 2009

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disease caused by infections with human influenza viruses. Complications that include pneumonia and death have been reported in the literature in otherwise healthy adults without underlying disease [3]. 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 [4].

Transmission

Although no extended transmission outside Mexico has been observed, limited transmission is reported from several countries. However, so far, the large majority of cases in Europe, USA or Canada have a history of travel to Mexico.

Virulence

It is still unexplained why the influenza A/H1N1 initially has seemed more virulent in Mexico than in the rest of the world. However, this difference may be disappearing when more data come in. Nonetheless, most of the cases diagnosed outside Mexico have had a mild disease, and hospitalizations have mainly occurred in patients with another underlying disease.

Laboratory diagnosis

Since this is a new influenza strain, the sensitivity of current techniques is low, resulting in false negative results. The first step in diagnosing human cases in the EU infected with this virus is to identify the presence of influenza A - as happened in Spain at the end of 2008 [5, 6]; specific methods (RT-PCR assays) for subtyping are under development in several European laboratories.

Testing of un-subtypable influenza A specimen for animal influenza strains by veterinary labs or the WHO Collaborating Centre for Reference and Research on Influenza in the UK, Mill Hills, could also identify the subtype H1N1 which includes this new genetic recombination in the virus.

The other reliable mean of confirming influenza A/H1N1 is virus isolation and sequencing of the virus genome. However this requires BSL 3 facilities.

Most influenza laboratories in the EU have now set up an RT-PCR to be able to identify the new virus, but they will need positive controls to calibrate their tests.

ECDC threat assessment for the EU

There are still scarce data on the characteristics that will decide the size, speed and seriousness of a potential pandemic.

Infectivity: We do not know if the virus transmits in the same way and with the same ease as common flu. At present, it seems as if transmission may be somewhat lower, but this assessment may change if more secondary/tertiary/etc. cases are diagnosed.

Reproduction rate: Unknown. We do not know how many new cases each case infects.

Immunity: We do not know if there is any immunity in the population from previous influenza infections. Serology studies should be performed after the first wave. Virus of the same subtype, A/H1N1, has been responsible for

seasonal flu during several years, but that subtype is quite different. Most of the genes of the virus are similar to genes that have developed in pigs –independently of human H1N1 viruses – probably since 1918.

Virulence: Unknown. We do not know what proportion of infected develop disease.

Spectrum of disease: Unknown, but there are probably many mild cases that will be difficult to differentiate from other respiratory tract infections.

Case fatality rate: Unknown, but judging from present data not higher than for seasonal influenza.

Age distribution: Unknown. We do not know if some age groups are more prone to becoming infected, to develop serious disease, or to die.

Susceptibility to antivirals: Based on in-vitro testing, we assume that oseltamivir and zanamivir will be equally efficacious for treatment of this virus as for other influenza strains.

In addition to close surveillance of cases in the EU, ECDC will continue to closely monitor the situation in Mexico and the US. It is mainly from these two countries that information to address the above issues will have to come. We will continuously provide information through our website and update this threat assessment as needed. For rapid updates, please see the Situation Reports published on our website (www.ecdc.europa.eu) every morning. 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 and capability to identify this new genetic composition is crucial. Clinicians need to consider seasonal and animal influenza in their differential diagnosis and ensure the necessary laboratory testing accordingly, especially in persons returning from affected areas. The collaboration between human and animal diagnostic labs is essential to ensure the identification of this new influenza virus and/or new virus strains as they are now appearing in Europe.

Contact

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