EMPRES WATCH
emergency prevention systems

The human influenza due to a novel subtype H1N1

Influenza viruses are RNA viruses belonging to the Orthomyxoviridae family, with "myxo" referring to the fact that they infect mucus membranes. The influenza viruses that cause human disease are divided into two types: A and B. Influenza A viruses can be classified into subtypes based on two surface proteins: hemagglutinin (H) and neuraminidase (N). At this time, 16 distinct haemagglutinins and 9 neuraminidases have been identified. Influenza A viruses can infect swine, equids, dogs, and other mammalian species, including humans, however, only birds have been found to host all of the hemagglutinin and neuraminidase combinations. The two subtypes which are most important causes of human influenza are A(H3N2) and A(H1N1), of which the former is currently associated with the greatest mortality.

Influenza viruses are known for their ability to change their antigenic structure and create new viral strains, possibly changing biological characteristics such virulence, infectivity or host range. Reassortments (gene segment exchange) between strains are frequent, and can mix viral RNA originating in different species. A new strain of H1N1 is currently spreading all over the world in the human population. According to virologists at the U.S. Centers for Disease Control and Prevention (CDC), the influenza A subtype H1N1isolated from these patients in April was a genetic reassortment of four different influenza virus strains, including human influenza gene segments, swine influenza from North America and Eurasia, and avian gene segments from North America, never before reported among swine or human isolates from anywhere in the world.

CONTENTS

1. REASSORTMENTS OF A NEW H1N1 STRAIN

Human influenza virus genes and avian influenza virus genes are known to reassort with swine influenza virus genes and enrich the gene pool of viruses circulating in pigs or human. As a result, genetic diversity of swine influenza viruses has increased over time, and the exchange of swine influenza virus genes circulating in Eurasia and the Americas may no longer be a rare event. In addition, the exchange of viral RNA can be a two-way street, with human influenza virus transmitted to pigs from their caretakers. Similarly, influenza virus can also be transmitted from poultry to pigs as well as from pigs to poultry. Through their ability to simultaneously host various influenza viruses, pigs may act as a "mixing vessel" for genetic reassortment of RNA from human, swine and avian viruses.

However, at the time of publication (30 April), no evidence had been found of clinical illness in the Mexican or US swine populations, and the virus had not been isolated from pigs or any other non-human species. We in FAO consider that the current H1N1 crisis has inappropriately been denominated "swine flu".

Major questions remained unanswered surrounding the origin of the different viral building blocks, the widely variable disease severity in suspect human patients in different locations and age groups, and how easily transmission may have been sustained in the various epidemiological and demographic settings around the world. An important characteristic of this outbreak was that the majority of the human patients seem to have little or no epidemiological links to pigs, strongly suggesting pure extended person-to-person transmission of this H1N1 virus.

2. SWINE INFLUENZA IS A COMMON AND WIDELY DISPERSED DISEASE OF PIGS

Swine influenza (SI) is caused by a number of influenza A viruses. The three subtypes that most commonly affect pigs are H1N1, H1N2 and H3N2. SI viruses are endemic in pig populations worldwide and are one of the most prevalent respiratory diseases in pigs.

- In North America, studies have shown that 30% of the entire American swine population has been exposed to H1N1 since 1930. Influenza vaccination is often part of herd health management systems. Reassortment is common, as illustrated by the fact that H3N2 subtypes with genes derived from influenza viruses of human, swine and avian origin have become a major cause of disease in pigs. In addition, H1N2 viruses resulting from reassortment between triple reassortant H3N2 viruses and clas-

History of swine influenza	
1918	Swine influenza H1N1 described in north central USA, Hungary, and China. May have been cause of human pandemic [19], which resulted in 20-40 million human deaths.
1930	Shope isolated influenza virus from pigs [33]. The prototype classic swine influenza H1N1 strain (A/Swine/Iowa/30) transmitted experimentally to pigs.
1941	Recognised in Europe and disappeared.
1970	Transmission of human H3N2 virus to pigs. Avian like H3N2 in pigs in Asia.
1976	Classical H1N1 reappears in European pigs.
1979	Introduction of whole H1N1 virus from birds to pigs. Antigenically distinguishable from classical strains. Still circulating today (2002).
1984	Reassortment between human H3N2 and avian H1N1 in swine resulting in reassortant H3N2 virus with avian internal gene segments [5]. H3N2 strains first associated with respiratory epizootics. Still circulating today (2002).
1986	Classical H1N1 reappears in UK, similar to classical H1N1 in continental Europe.
1987	Reassortant H3N2 associated with respiratory epizootics in UK. Related to A/Port Chalmers/73 (H3N2).
1989	Avian like swine H1N1 is dominant and widespread in Europe.
1992-1993	Avian like H1N1 strains widespread in UK.
1993	Infection of children with reassortant H3N2 virus from pigs and isolation of avian like swine H1N1 virus from a pneumonia patient in the Netherlands.
1994	H1N2 first isolated in pigs in UK, and later also in Belgium. Human avian reassortant virus [3, 37].
1992-1998	H3N1 (H3 human, N1 swine) and H1N7 (H1 human, N7 equine) also occurred in swine in the UK but failed to spread.
1998	H9N2 in pigs and humans in Asia [17]. Apparently an avian virus that has adapted to pigs.
1998	For the first time, H3N2 viruses cause severe disease in N. America. Viruses are triple (avian human classical swine) reassortants, distinct from earlier strains and European strains. H1N2 identical to H3N2, but with H1HA from classical swine H1N1, also isolated.
1999	Single case of isolation of avian H4N6 from pigs with pneumonia in Canada.
2002	Current situation in Europe: avian like H1N1, and reassortant human like H3N2 and H1N2. In North America: classical swine H1N1, triple reassortant H3N2.

From: Salient points in the history of swine influenza (adapted from Done and Brown, 1999), *from Swine influenza: a zoonosis, Paul Heinen*

sical H1N1 swine viruses have been isolated from pigs in at least six states.

- In Europe, recent monitoring by the European Surveillance Network for Influenza in Pigs (ESNIP2) has shown that subtypes H1N1, H3N2 and H1N2 co-circulate in pig populations. Differences between countries do exist. For example, swine H1N1 viruses co-circulate with H1N2 in the United Kingdom, where H3N2 apparently disappeared in the mid-1990s

The disease in swine has a strong economic impact on the pig industry in industrial farming systems in the UK alone, SI costs have been estimated at up to £7 per pig, accounting for a financial loss to the pig industry of approximately £65 million each year.

Signs of the disease in pigs

SI in pigs is characterized by fever, coughing, sneezing, nasal discharge, and respiratory difficulty. Reproductive problems including abortion can also be found. While all swine in a herd may become sick, case mortality rates are generally low. The virus is usually transmitted through nasal discharge and aerosol from coughing or sneezing.

Infection in humans

Swine flu viruses do not infect humans very frequently, and SI in humans is associated with direct and close contact with infected pigs. Until the recent H1N1 event (April 2009), most swine influenza in humans was associated with occupational exposure, such as workers in the pig or poultry industries. Most of the patients recovered swiftly and there were few fatalities.

The signs and symptoms found in humans infected with SI viruses resemble seasonal influenza, i.e. fever, lethargy, lack of appetite and coughing. Some patients have also reported runny nose, sore throat, nausea, vomiting and diarrhea.

Control of the disease

Control measures to stop SI virus spread in the pig population consist mainly of movement control and biosecurity. Good personal and environmental hygiene and sanitation practices will inactivate influenza viruses and/or remove them from the environment. The influenza viruses, such as H1N1, are quickly destroyed by soap and detergents.

Vaccination is often practiced in developed countries. Pig vaccines are bivalent (H1N1 and H3N2). As with many influenza vaccines, changes in the circulating viral subtypes may lead to vaccines not conferring protection to the circulating SI virus.

3. FAO RESPONSE

FAO considers these latest reports on the new influenza A subtype H1N1 infections in humans to be a cause for concern. The virus had rapidly traveled over long distances, crossing three continents and affecting groups of persons in several countries by the time active surveillance was initiated. The seasonal human influenza vaccine was not expected to confer strong protection against this novel swine flu virus, according to the CDC. CDC and the World Health Organization (WHO) reported that the first viruses isolated were susceptible to the newer influenza antivirals: oseltamivir (Tamiflu®) and zanamivir (Relenza®), but not to the older ones, amantadine and rimantadine.

Despite increased pig and poultry surveillance activities particularly in Europe and Northern America, there is as yet not intensive enough surveillance systems in place to provide precise information on the extent and evolution of influenza virus circulation in pigs and poultry around the world. Following the spread of the highly pathogenic H5N1 avian influenza in poultry in Asia, Europe and Africa, efforts have been strengthened considerably through the joint OIE and FAO reference laboratory network for influenza viruses (OFFLU), but much work remains to be done before we can effectively monitor worldwide trends of influenza virus transmission among domestic animals and humans.

FAO EMPRES and the FAO/OIE Crisis Management Centre-Animal Health (CMC-AH) are closely working with the global network of FAO country, Sub-Regional and Regional Offices. FAO staff around the world will remain vigilant, gather epidemiologic data, report unusual influenza-like illness in swine, assist in facilitating the forwarding of appropriate specimens to international influenza reference laboratories and respond to urgent health needs. Through the FAO/OIE/WHO Global Early Warning System (GLEWS), timely data and information are shared between the three international organisations, which communicate and coordinate with other partners, including the World Bank, FAO/OIE reference laboratories, the CDC, USDA/APHIS and key national and academic institutions.

The CMC-AH deployed a mission to Mexico to support authorities' efforts to address issues related to the pig sector. Particularly, the mission will provide technical advice regarding any possible recent or new disease events in pigs, as well as on biosecurity and laboratory analysis. Moreover, the team will support animal-human interface analysis, in cooperation with the Veterinary Services and Public Health teams.

FAO, with its partners, will continue to assist member countries to gain a comprehensive understanding of influenza virus circulation at the human-animal interface, including pigs and poultry. The current situation calls for stepping up global virus surveillance programmes and efforts to understand the ecology of influenza virus transmission within and between species, putting the One World/One Health model into practice.

4. CONCLUSION

At this time, there is no evidence that this novel influenza virus is circulating in the animal population and it is currently not known where and when the reassortment that led to the emergence of this virus occured. Investigations by national and international health agencies are ongoing, and should lead to a better understanding of the epidemiological situation.

Our understanding of the prevalence of usual swine influenza is limited at this time. SI is not included in list of notifiable diseases of pigs, and SI surveillance is not routinely done in many countries. Given the recent emergence of the new H1N1 virus as a significant cause of illness, FAO recommends that countries carry out surveys to determine the extent and intensity of all possible influenza virus type A circulation, with specific reference to subtypes H1N1, H1N2 and H3N2.

Countries that are affected by or are at high-risk from H5N1 highly pathogenic avian influenza infection, should not lift or shift their ongoing prevention, detection, and control measures to protect avian species and humans. The recommendations of FAO, OIE, and WHO remain.

5. FOR MORE INFORMATION

Information on confirmed human cases of new influenza A subtype H1N1 infections and the WHO response to outbreak is available on the WHO website: http://www.who.int/csr/disease/swineflu/en/index.html

OIE statements: http://www.oie.int/eng/en_index.htm

A fact sheet presenting general information on influenza -including swine influenza- is available at the following link: http://www.cfsph.iastate.edu/Factsheets/pdfs/influenza.pdf

Information on European Surveillance Network for Influenza in Pigs (ESNIP) project of DG Research, EC is available on the following website: http://www.esnip.ugent.be/