

## 田代委員提出資料

**J Virol. The M segment of the 2009 new pandemic H1N1 influenza virus is critical for its high transmission efficiency in the guinea pig model.**

[Source: US National Library of Medicine, full text: ([LINK](#)). Abstract, edited.]

J Virol. 2011 Aug 31. [Epub ahead of print]

**The M segment of the 2009 new pandemic H1N1 influenza virus is critical for its high transmission efficiency in the guinea pig model.**

Chou YY, Albrecht RA, Pica N, Lowen AC, Richt JA, García-Sastre A, Palese P, Hai R.

**Source**

Department of Microbiology.

**Abstract**

A remarkable feature of the 2009 pandemic H1N1 influenza virus is its efficient transmissibility in humans compared to precursor strains from the triple reassortant swine influenza virus lineage, which cause only sporadic infections in humans. The viral components essential for this phenotype have not been fully elucidated. In this study, we aimed to determine the viral factors critical for aerosol transmission of the 2009 pandemic virus. Single or multiple segment reassortments were made between the pandemic A/California/04/09 (H1N1) [Cal/09] virus and another H1N1 strain A/Puerto Rico/8/34 (H1N1) [PR8]. These viruses were then tested in the guinea pig model to understand which segment of Cal/09 virus conferred transmissibility to the poorly transmissible PR8 virus. We confirmed our findings by generating recombinant A/swine/Texas/1998 (H3N2) [sw/Tx/98] virus, a representative triple reassortant swine virus, containing segments of the Cal/09 virus. The data showed that the M segment of the Cal/09 virus promoted aerosol transmissibility to recombinant viruses with PR8 and sw/Tx/98 virus backgrounds, suggesting that the M segment is a critical factor supporting the transmission of the 2009 pandemic virus.

PMID:

21880744

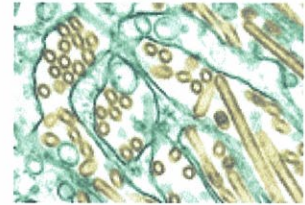
[PubMed - as supplied by publisher]



## "Have You Heard?"

Archive: 2010 | [2009 \(/media/haveyouheard/2009.html\)](/media/haveyouheard/2009.html) | [2008 \(/media/haveyouheard/2008.html\)](/media/haveyouheard/2008.html)

Recent media coverage stemming from a Food and Agriculture Organization (FAO) [press release \(http://www.fao.org/news/story/en/item/87196/icode/\)](http://www.fao.org/news/story/en/item/87196/icode/) has contained misleading information about highly pathogenic avian influenza A (H5N1) viruses ("H5N1") in Asia. Some of that media coverage has implied that there is a new, mutant variant H5N1 virus that is spreading in Asia, and that the risk to human health posed by this H5N1 virus has somehow been recently and dramatically raised. This is not true.



Highly pathogenic (deadly) avian influenza A (H5N1) virus infections in poultry and wild birds, resulting in high mortality, have been detected in Asia, the Middle East, Europe, and Africa since December of 2003. Currently, H5N1 viruses are widespread in poultry and wild birds in many countries in Asia, but rarely infect humans. When humans become ill with H5N1 virus infection, severe illness and death may occur. Sporadic human cases mainly occur after contact with infected poultry that were sick or dead, and have been reported in 15 countries. Like all influenza viruses, H5N1 viruses continue to evolve. The [Centers for Disease Control and Prevention \(CDC\) \(http://www.cdc.gov/flu/weekly/overview.htm\)](http://www.cdc.gov/flu/weekly/overview.htm), the [World Health Organization \(http://www.who.int/en/\)](http://www.who.int/en/) (WHO), [World Organization for Animal Health \(http://www.oie.int/\)](http://www.oie.int/) (OIE), and [Food and Agriculture Organization \(http://www.fao.org/\)](http://www.fao.org/) of the United Nations (FAO) conduct routine surveillance to monitor influenza viruses, including H5N1 viruses, for changes that may have implications for animal and public health. CDC and WHO surveillance efforts are geared toward human health. FAO and OIE are concerned with issues affecting food and agriculture.

Over time, H5N1 viruses have evolved into different groups, called "clades." Since 2007, 12 different clades of H5N1 viruses have been identified. The FAO report and subsequent media stories focused on an H5N1 virus that has been given a nomenclature (name) of "clade 2.3.2.1". However, this virus is not new. It was first detected in poultry during 2009 in Vietnam and evolved from viruses that had previously been circulating in Vietnam since 2005.

CDC has been watching the evolution of all H5N1 viruses closely. Changes in viruses that WHO and CDC look for specifically are those that could increase the threat to human health. There is nothing to indicate that clade 2.3.2.1 viruses pose any greater threat to human health than any of the other H5N1 viruses. The clade 2.3.2.1 viruses are very active viruses and are spreading more widely in poultry and wild birds. While this increases the possibility of human exposures to infected birds or poultry, it does not increase their ability to infect and transmit between people. However, as part of the U.S. government's pandemic preparedness activities, a 2.3.2.1 vaccine virus candidate to protect humans against this virus already has been created so that vaccine production could begin rapidly if this virus were to change to infect humans and spread easily from person to person. The vaccine virus candidate is an exact match to currently circulating 2.3.2.1 viruses.

CDC does not believe the risk from H5N1 to humans has increased; however, the evolution of H5N1 viruses has implications for the poultry industry in parts of the world where H5N1 viruses are widespread among poultry. In many of these countries, poultry is routinely vaccinated to protect against infection with H5N1 viruses, which is frequently deadly to them. Vaccination of poultry against avian influenza viruses is a tool used to protect a food asset. The FAO report was drawing attention to the fact that the H5N1 poultry vaccines currently being used in Vietnam do not protect poultry against the new H5N1 clades. This is because the viruses have evolved since the H5N1 poultry vaccine viruses were chosen in 1996. While this development highlights the importance of updating the antigen composition of all influenza vaccines, it does not have any bearing on the issue of protecting humans from this virus.

In summary, H5N1 influenza viruses have been circulating among birds for many years, some are highly pathogenic, and infections in humans are uncommon. There have been no recent changes that pose any additional risk to humans.

More information on avian influenza can be found on the [WHO website \(http://www.who.int/csr/disease/avian\\_influenza/en/index.html\)](http://www.who.int/csr/disease/avian_influenza/en/index.html) at [http://www.who.int/csr/disease/avian\\_influenza/en/index.html](http://www.who.int/csr/disease/avian_influenza/en/index.html) ([http://www.who.int/csr/disease/avian\\_influenza/en/index.html](http://www.who.int/csr/disease/avian_influenza/en/index.html))

- Historical Document: 2011
- Content source: [Office of the Associate Director for Communication \(mailto:media@cdc.gov&subject=Newsroom:%20Website\)](mailto:media@cdc.gov)
- Notice: Links to non-governmental sites do not necessarily represent the views of the CDC.





## RAPID RISK ASSESSMENT

# Potential resurgence of highly pathogenic H5N1 avian influenza

September 2011

### Conclusions and recommendations:

The increased reports of A(H5N1) outbreaks in poultry and wild bird populations, and the emergence of a further evolved lineage of the virus in poultry in some countries, do not change the current assessment of the risk to human health. This is still considered to be very low in EU/EEA countries. However, vigilance for avian influenza in domestic poultry and wild birds in Europe remains important.

In the countries where A(H5N1) is entrenched in wild bird populations and is occasionally transmitted to domestic poultry, rare and sporadic human infections in individuals who have contact with this poultry (or wild birds) are to be expected and should be considered as background cases. Constant vigilance should be maintained for any enlargement in A(H5N1) cluster size or for individual human cases outside of the countries where the virus is entrenched in poultry.

### Source and date of request

Internal ECDC decision, 30 August 2011.

### Public health issue

Report to the media from the Food and Agriculture Organization of the United Nations (FAO) on 29 August 2011, warning of a possible resurgence of highly pathogenic avian influenza A(H5N1) and the emergence of a new variant of the virus (H5N1 2.3.2.1) in China and Viet Nam, not necessarily covered by the existing vaccines for poultry.

### Consulted experts

Elizabeth Mumford – World Health Organization

Timm Harder, David Swayne, Ian Brown – OFFLU OIE/FAO Network of expertise on animal influenza

Juan Lubroth – FAO

Marion Koopmans – RIVM (National Institute for Public Health and the Environment), the Netherlands.

## Disease background information

Influenza virus type A(H5N1) is a group of avian viruses that are highly pathogenic and very infectious for a number of bird species, including most domestic poultry species kept by humans. Since 1997, the highly pathogenic avian influenza (HPAI) virus A(H5N1) has affected poultry, initially in the Far East and later in parts of Europe, the Middle East and Africa. The infection is considered entrenched at least in parts of Bangladesh, China, Cambodia, Egypt, India, Indonesia and Viet Nam and has been reported intermittently in other countries. In Europe, the latest recorded events date from 2010, when a large number of wild birds were found dead in the Tyva Republic of the Russian Federation, two backyard poultry outbreaks occurred in Romania and a common buzzard tested positive for the virus in Bulgaria. No events have been reported in 2011 so far.

To date, the virus is poorly adapted to the human species so that it only rarely causes illness in those exposed to it. For the few people that do become infected, the A(H5N1) virus can be highly virulent and the mortality rate has been significant (over 50%). Although human-to-human transmission has occurred, it is as yet inefficient (the R0 is well under one) which also reflects the poor adaptation of the virus to humans.

Since 2003, and as of 19 August 2011, 565 human cases with 331 deaths (fatality rate 58.6%) have been reported to the World Health Organization (WHO). These confirmed human cases of avian influenza A(H5N1) have been reported in 15 countries. The majority of cases occurred in the major risk group of people who have contact with domestic poultry, especially in households or contaminated environments. So far during 2011 (as at 19 August) WHO has reported 49 cases and 25 deaths from four different countries: Bangladesh (two cases – no deaths), Cambodia (eight cases – eight deaths), Egypt (32 cases – 12 deaths) and Indonesia (seven cases – five deaths). No clusters have been reported in 2011, apart from two mother and child pairs, one in Indonesia and one in Cambodia, probably due to dual environmental exposure.

## Event background information

On 29 August, the Food and Agriculture Organization of the United Nations (FAO) published a press release warning of 'a possible major resurgence of the H5N1 Highly Pathogenic Avian Influenza amid signs that a mutant strain of the deadly Bird Flu virus is spreading in Asia and beyond, with unpredictable risks to human health'. The article refers to an increase in the number of outbreaks in domestic poultry and wild bird populations since July 2008, mainly in Asian countries, after a steady decrease had been noted in the previous period.

## ECDC Rapid Risk Assessment for the European Union

The true level of infection and distribution of A(H5N1) among poultry and wild birds is difficult to determine because of inherent weaknesses in surveillance and laboratory capacity in many countries, especially those with limited resources. The same applies to human cases.

It is recognised that any apparent increase in the number of outbreaks in domestic poultry and wild bird populations or changes in the distribution of the outbreaks is important and needs to be monitored. However, from a human health perspective, there are currently no indications of any significant change in the human epidemiology associated with any clade or strain of A(H5N1). This is based on the absence of human-to-human transmission, and on the observation that there is no apparent change in the size of clusters or reports of chains of infection. For this reason, the conclusions from the risk assessment published by ECDC in 2006 remain valid. The main points are:

- Transmissibility of A(H5N1) viruses to humans is still considered very low, requiring high infectious doses or some other, as yet unknown, variable;
- There is no evidence of the virus having become more adapted to humans;
- The direct risk to the health of the European population from A(H5N1) is very low and is mainly concentrated in persons with domestic or pet poultry.

The reported emergence of a new lineage of A(H5N1) follows the pattern observed since the first detection of these particular viruses in 1995. Since then, A(H5N1) viruses have evolved into different lineages, reflecting the widespread occurrence of infections in animals. This stresses the importance of adequate surveillance, regardless of the vaccination status of animals.

In EU Member States surveillance for highly pathogenic avian influenza in poultry is strong and is carried out on a continuous basis. ECDC is closely monitoring the situation, both in the EU and worldwide, and will regularly reassess the potential for a change in the A/H5N1 risk to humans.

## Conclusions

Any recently observed increase in the number of outbreaks in poultry and wild bird populations and the emergence of different lineages of the virus does not change the current EU risk assessment in relation to highly pathogenic avian influenza A(H5N1) in humans and this risk is still considered to be very low.

## Contact

[support@ecdc.europa.eu](mailto:support@ecdc.europa.eu)

## References

European Centre for Disease Prevention and Control (ECDC). The public health risk from highly pathogenic avian influenza viruses emerging in Europe with specific reference to type A/H5N1. Version: 1 June 2006. Available from: [http://ecdc.europa.eu/en/publications/Publications/0606 TER The Public Health Risk from Highly Pathogenic Avian Influenza Viruses Emerging in Europe.pdf](http://ecdc.europa.eu/en/publications/Publications/0606_TER_The_Public_Health_Risk_from_Highly_Pathogenic_Avian_Influenza_Viruses_Emerging_in_Europe.pdf)

ECDC factsheet for professionals for avian influenza. Available from: [http://ecdc.europa.eu/en/healthtopics/avian\\_influenza/basic\\_facts/Pages/factsheetf\\_professionals.aspx](http://ecdc.europa.eu/en/healthtopics/avian_influenza/basic_facts/Pages/factsheetf_professionals.aspx)

Fiebig L, Soyka J, Buda S, Buchholz U, Dehnert M, Haas W. Avian influenza A(H5N1) in humans: new insights from a line list of World Health Organization confirmed cases, September 2006 to August 2010. *Euro Surveill.* 2011;16(32):pii=19941. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19941>

Food and Agriculture Organisation (FAO), Media Centre. Bird flu rears its head again. 29 August 2011. Available from: <http://www.fao.org/news/story/en/item/87196/icode/>

Food and Agriculture Organisation (FAO). H5N1 HPAI Global overview: April–June 2011. Available from: <http://www.fao.org/docrep/014/am722e/am722e00.pdf>

Nicoll A. (Yet) another human A/H5N1 influenza case and cluster – when should Europe be concerned? *Eurosurveillance* 2008; Volume 13, Issue 15, 10 April 2008. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18833>

Tarantola A, Barboza P, Gauthier V, Ioos S, El Omeiri N, Gastellu-Etchegorry M, for the Epidemic Intelligence team at InVS. The influenza A(H5N1) epidemic at six and a half years: 500 notified human cases and more to come. *Euro Surveill.* 2010;15(29):pii=19619. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19619>

World Health Organization (WHO). Confirmed Human Cases of Avian Influenza A(H5N1). Available from: [http://www.who.int/csr/disease/avian\\_influenza/country/en/index.html](http://www.who.int/csr/disease/avian_influenza/country/en/index.html)

INFLUENZA (50): AUSTRALIA (NEW SOUTH WALES), H275Y MUTATION CLUSTER

\*\*\*\*\*

A ProMED-mail post

<<http://www.promedmail.org>>

ProMED-mail is a program of the International Society for Infectious Diseases

<<http://www.isid.org>>

Date: Thu 24 Aug 2011

From: Kate Hardie <[Kate.Hardie@hnehealth.nsw.gov.au](mailto:Kate.Hardie@hnehealth.nsw.gov.au)>

A cluster of oseltamivir-resistant A(H1N1)2009 influenza cases with onset between May and August 2011 has been detected in the Hunter region of New South Wales (NSW), Australia.

Viruses from 25 of 184 (14 percent) A(H1N1)2009 cases from the Hunter New England region exhibited highly reduced oseltamivir sensitivity due to the H275Y substitution in the neuraminidase. The H275Y mutation is a well-established substitution previously reported to confer oseltamivir resistance in N1 neuraminidases and was present in the widespread oseltamivir resistant pre-pandemic seasonal A(H1N1) virus.

15 of the 1st 16 cases lived within a 50-km radius of the regional centre of Newcastle. 16 of the 25 patients have been interviewed, and none had received oseltamivir prior to influenza specimen collection. Only 5 were hospitalised at the time of specimen collection. None of the 16 had a history of immune suppression; 3 cases were pregnant. No one was admitted to ICU or had a fatal outcome. Further interviews with cases and virological analyses are ongoing.

---

Communicated by:

Kate Hardie

Hunter New England Population Health

NSW, Australia

<[Kate.Hardie@hnehealth.nsw.gov.au](mailto:Kate.Hardie@hnehealth.nsw.gov.au)>

Aeron Hurt

WHO Collaborating Centre for Reference and Research on Influenza

Melbourne, Australia

Noelene Wilson

Nicole Gehrig Hunter Area Pathology Service

NSW, Australia

[ProMED-mail thanks Kate Hardie and colleagues for communicating the discovery of this cluster of oseltamivir-resistance cases in the Hunter region of New South Wales.

According to the most recent WHO weekly update on oseltamivir resistance in influenza A(H1N1)2009 viruses, dated 13 Jul 2011, the cumulative total of cases since April 2009 was 565. It was concluded that the overall incidence of viruses resistant to antivirals remained very low, with no recent reports of case clusters. The preceding report from New South Wales is significant in this respect.

A map of the Hunter Valley region of New South Wales can be accessed at: <<http://www.sydney-australia.biz/maps/hunter-valley-map.php>>. -Mod.CP]

[see also: Influenza (44): WHO update 20110716.2155]