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REGIONAL OFFICE FOR **Europe**

## **WHO Regional Office for Europe update on avian influenza A(H7N9) virus**

Situation update 3: 9 May 2013

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*This update summarizes the available information and recommendations made by WHO about human infections with avian influenza A(H7N9) virus in China for Member States of the WHO European Region.*

WHO/Europe emphasizes the need for Member States to maintain the capacity to detect any unusual health event, including those that may be associated with a new subtype of influenza A which should be notified to WHO in accordance with the International Health Regulations (2005). Human health and animal health sectors should maintain close and systematic interactions for timely exchange of information and to conduct joint risk assessments for the prevention and control of zoonotic diseases, as necessary. This work should be done under the relevant components of multi-hazard plans for preparedness and response to public health events.

WHO/Europe is coordinating its activities related to this outbreak with the European Commission, the European Centre for Disease Prevention and Control (ECDC), the EuroFlu network ([www.euroflu.org](http://www.euroflu.org)) and the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL).

This update is posted every week in English and (with a possible slight delay for translation) in Russian and includes:

- a situation update;
- latest WHO risk assessment (this week as of 13 April 2013);
- recommendations; and
- key references and guidance.

### **What is new in this update?**

- Five additional laboratory confirmed cases and eight new deaths reported from China since the previous WHO/Europe update on 30 April 2013.
- In total 131 cases and 32 deaths have been reported from China National Health and Family Planning Commission and the Tapei CDC.
- Publication of WHO Vaccine Response to the avian influenza A(H7N9) outbreak – step 1: development and distribution of candidate vaccine virus (2 May 2013). See section 1 under *prevention* in this update.
- Summary of joint China National Health and Family Planning Commission and WHO mission on A(H7N9).

## **1) Situation update**

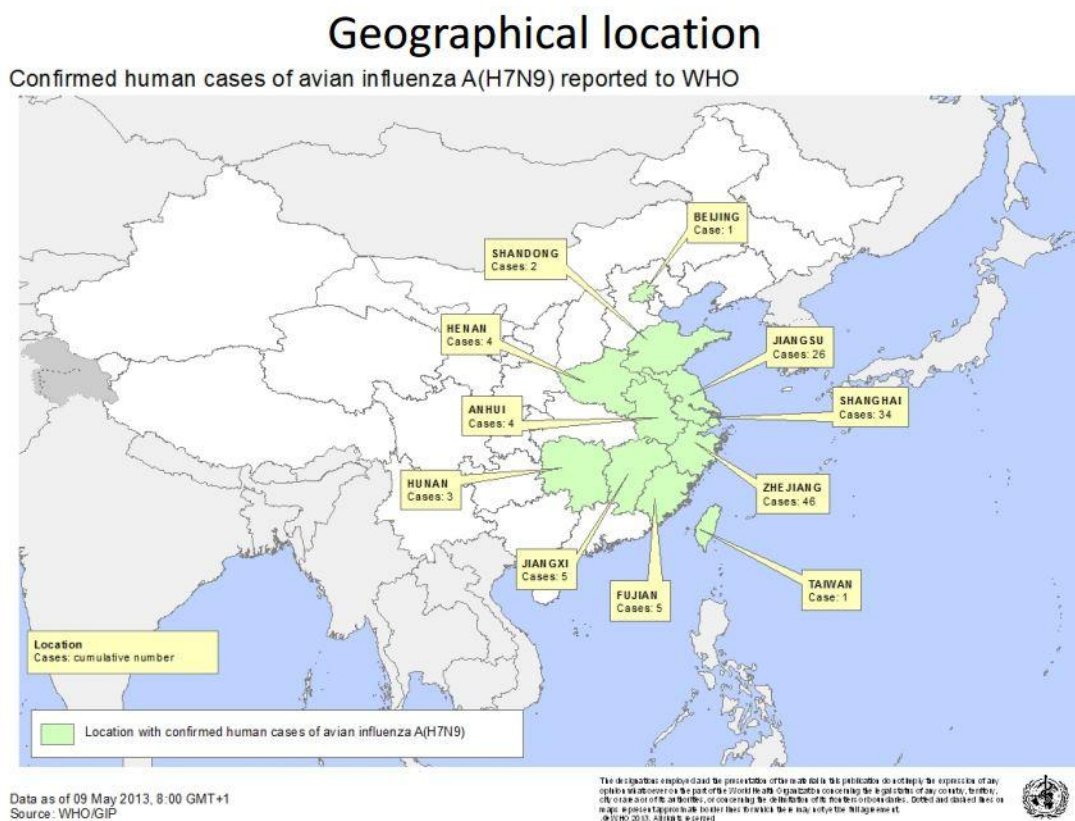
On 31 March 2013, the health authorities of China notified WHO of three laboratory-confirmed human cases of avian influenza A(H7N9) virus infection. These cases reported from China are the first known cases of human infection with A(H7N9). Since that time China has continued to report new human cases. As of 9 May 2013, 130 laboratory confirmed human cases with A(H7N9) virus including 32 fatalities in China have been reported from eight provinces (Anhui, Fujian, Henan, Hunan, Jiangsu, Jiangxi, Shandong and Zhejiang) and two municipalities (Beijing and Shanghai). In addition, one case has been reported from Tapei Centers for Disease Control.

### WHO expert mission to China

A joint China National Health and Family Planning Commission and WHO team of international and Chinese influenza experts carried out a mission to China on 16–23 April 2013 visiting laboratories, hospitals, clinics, markets and affected areas in Shanghai. It was found that the response by the Chinese government is being carried out with strong leadership and a high level of commitment. The strategies implemented such as health education, communication and closure of live poultry markets were found sound and effective. The mission team came up with a number of recommendations for the prevention and control of A(H7N9), which can be found here:

<http://www.wpro.who.int/china/mediacentre/speeches/2013/20130424/en/index.html>

The following map, table of confirmed cases and epidemiological curve were published by WHO headquarters in the weekly report *Number of confirmed human cases for avian influenza A(H7N9) reported to WHO* as of 9 May 2013.<sup>1</sup>



<sup>1</sup> Number of confirmed human cases of avian influenza A(H7N9) reported to WHO [web site]. Geneva, World Health Organization, ([www.who.int/influenza/human\\_animal\\_interface/influenza\\_h7n9/Data\\_Reports/en/index.html](http://www.who.int/influenza/human_animal_interface/influenza_h7n9/Data_Reports/en/index.html), accessed 10 May 2013).

## Cumulative number of confirmed cases of avian influenza A(H7N9) reported to WHO, by month, 2013

Total	February		March		April		May		unknown month of onset		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
	2	2	30	12	87	7	2	0	10	11	131	32

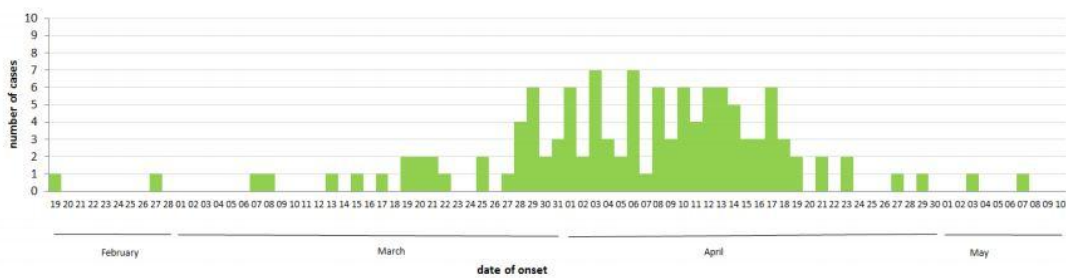
Total number of cases includes number of deaths  
WHO reports only laboratory cases  
All dates refer to onset of illness

Data in WHO/HQ as of 09 May 2013, 08:00 GMT+1  
Source: WHO/GIP



## Epidemiological curve of confirmed cases of avian influenza A(H7N9) reported to WHO, by day, 2013

**N = 121 confirmed cases for whom date of onset is known**



All dates refer to onset of illness

Data in WHO/HQ as of 09 May 2013, 08:00 GMT+1  
Source: WHO/GIP



See also: *Disease Outbreak News*, WHO headquarters, [www.who.int/csr/don/en/index.html](http://www.who.int/csr/don/en/index.html)

### *Infections with avian influenza A(H7N9) virus and epidemiology*

Although these cases reported from China are the first known cases of human infection with an avian influenza A(H7N9) virus, this virus is one subgroup among the larger group of influenza A(H7) viruses which have previously been reported to cause sporadic human infections associated with poultry outbreaks. These infections in humans have mainly resulted in mild disease (e.g. conjunctivitis and mild upper respiratory symptoms). In contrast, many of the reported cases of human infection with avian influenza A(H7N9) virus have resulted in severe disease and deaths.

The source of infection and the mode of transmission for the A(H7N9) virus are currently unknown. Small clusters that may indicate limited human-to-human transmission have been detected, but there is no evidence of sustained, efficient human-to-human transmission. More than 1000 close contacts of confirmed cases and health care workers providing care for patients infected with A(H7N9) have been monitored by public health authorities for infection and have not developed clinical disease.

This virus has now also been isolated from poultry (including ducks and pigeons) in live bird markets in some areas of China. National and international human and animal health authorities are working hard to determine the source of infection. This work is complicated by the fact that so far this virus has not been associated with reports of severe disease in poultry and appears to be a low pathogenicity avian influenza (LPAI) virus.<sup>2</sup> Investigations are ongoing to determine if any animal reservoir of this virus exists, including other domestic and wild bird species, and mammalian species such as swine.

### *Clinical presentation*

The main clinical feature among most avian influenza A(H7N9) patients has been respiratory disease resulting in severe pneumonia. Symptoms include fever, cough and shortness of breath. Many of the reported patients have required intensive care and mechanical ventilation. Only a few of the cases have reported mild disease. Investigations are ongoing to determine the full spectrum of disease associated with avian influenza A(H7N9) infection.

### *Virology*

The virus contains a group of avian influenza virus genes from three different avian influenza viruses. The gene for the haemagglutinin or HA protein belongs to a Eurasian group of H7 avian influenza viruses, but is genetically distinct. The gene for the neuraminidase or NA protein is similar to avian A(H11N9) viruses found in South Korea in 2011, in Hongze, Jiangsu, China in 2010 and in the Czech Republic in 2005. The 6 genes coding for the internal proteins are similar to recent A(H9N2) viruses found in China and South Korea. Influenza A(H9N2) viruses are endemic in birds, including poultry, in Asia and elsewhere. Sequence analyses have shown that the genes of the influenza A(H7N9) viruses show signs of adaption to growth in mammalian species. These adaptations include an ability to bind to mammalian cell receptors, and to grow at temperatures close to normal body temperature of mammals (which is lower than that of birds).<sup>34</sup>

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<sup>2</sup> Understanding avian influenza: Current state of knowledge on Highly Pathogenic Avian Influenza [web site]. Rome, Italy, Food and Agriculture Organization of the United Nations (FAO) ([http://www.fao.org/avianflu/documents/key\\_ai/key\\_book\\_ch2.htm](http://www.fao.org/avianflu/documents/key_ai/key_book_ch2.htm), accessed 22 April 2013).

<sup>3</sup> Public health relevant virological features of influenza A(H7N9) causing human infection in China [web site]. Copenhagen, Denmark, World Health Organization Regional Office for Europe. (<http://www.euro.who.int/en/what-we-do/health-topics/communicable-diseases/influenza/publications/2013/public-health-relevant-virological-features-of-influenza-ah7n9-causing-human-infection-in-china>, accessed 22 April 2013).

### *Treatment*

Laboratory tests have shown that avian influenza A(H7N9) viruses are sensitive to the neuraminidase inhibitors class of influenza drugs (oseltamivir and zanamivir), but resistant to the antiviral drugs amantadine and rimantadine. When antiviral drugs are given early in the course of illness, they have been found to be effective against seasonal influenza virus and influenza A(H5N1) virus infection. Treatment should still be initiated >48hrs after symptom onset if the patient has severe disease or is deteriorating.

### *Prevention*

No vaccine is currently available, but the viruses from the initial cases have been isolated and characterized with the aim to select candidate viruses for the vaccine. WHO and its partners will continue to characterize available viruses to identify the best candidate viruses to be used should a need for global vaccine production arise. On 2 May WHO published the Vaccine Response to the avian influenza A(H7N9) outbreak – step 1: development and distribution of candidate vaccine virus, which describes the process of selecting a candidate vaccine virus as well as its release. In order to enhance vaccine production readiness, it has been decided to release the potential reassortant candidate vaccine virus if certain criteria are fulfilled. The potential reassortant candidate vaccine virus is expected to be available soon and vaccine manufacturers, research institutes and other interested bodies can request the virus by sending an e-mail to the WHO Collaborating Centres for Influenza and Essential Regulatory Laboratories of the Global Influenza Surveillance and Response System (GISRS) as listed at:

[http://www.who.int/influenza/gisrs\\_laboratory/collaborating\\_centres/list/en/index.html](http://www.who.int/influenza/gisrs_laboratory/collaborating_centres/list/en/index.html). The full document can be accessed at [http://www.who.int/influenza/vaccines/virus/CandidateVaccineVirusesH7N9\\_02May13.pdf](http://www.who.int/influenza/vaccines/virus/CandidateVaccineVirusesH7N9_02May13.pdf)

WHO/Europe would like to emphasize that while the source of infection and the mode of transmission have not yet been determined, it is prudent to follow good hygiene practices to prevent infection. For advice on infection prevention, contact with animals and food preparation, see:

[http://www.who.int/influenza/human\\_animal\\_interface/faq\\_H7N9/en/](http://www.who.int/influenza/human_animal_interface/faq_H7N9/en/).

Guidance for infection prevention and control in health care settings is available at

[http://www.who.int/csr/resources/publications/swineflu/WHO\\_CDS\\_EPR\\_2007\\_6/en/index.html](http://www.who.int/csr/resources/publications/swineflu/WHO_CDS_EPR_2007_6/en/index.html).

## **2) WHO risk assessment as of 13 April 2013**

There are several critical gaps in information at this stage, including lack of knowledge about the animal reservoir(s) in which this virus is likely circulating, the main exposures and routes of transmission for humans and the current extent of spread of the A(H7N9) virus among animal and human populations. The current WHO risk assessment published on 13 April 2013, can be summarized as follows:

### **I. Risk of the occurrence of further cases in the affected areas of China and other areas**

The epidemiology of the A(H7N9) virus among animals, including the main reservoirs of infection among animals and the extent of geographic spread, is not yet established. However, it is likely that most human A(H7N9) infections so far are associated with contact to infected animals, and further human cases of infection should be expected.

### **II. Risk of human-to-human transmission**

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<sup>4</sup> Liu D, Shi W, Shi Y, Wang D, Xiao H, Li W, et al. Origin and diversity of novel avian influenza A H7N9 viruses causing human infection: phylogenetic, structural, and coalescent analyses. In: Lancet. 2013/05/07 ed. Available at: <http://www.sciencedirect.com/science/article/pii/S0140673613609381>.



There is no evidence of sustained human-to-human transmission. However, the two possible family clusters suggest that limited human-to-human transmission may occur where there is close contact between cases and other individuals, as occurs in families and, potentially, health care settings. Moreover, the genetic changes seen among these viruses suggesting adaptation to mammals is of concern, and further adaptation may occur.

### III. Risk of international spread

At this time, there is no evidence to indicate international spread of this virus. It is possible that A(H7N9) could be imported into other countries through infected travellers or animals, who may or may not display symptoms. However, if the virus cannot sustain human-to-human transmission, as appears to be the current situation, then extensive community spread is unlikely.<sup>5</sup>

## 3) Recommendations

WHO/Europe reemphasizes the need for Member States to maintain the capacity to detect any unusual health event, including those that may be associated with a new subtype of influenza A, in accordance with the International Health Regulations (2005). Human health and animal health sectors should maintain close and systematic interactions for timely exchange of information and conduct joint risk assessments for the prevention and control of zoonotic diseases, as necessary. This work should be done under the relevant components of multi-hazard plans for preparedness and response to public health events.

Member States are encouraged to conduct national risk assessment, and update and implement the relevant components of multi-hazard plans for preparedness and response based on available information. A list of relevant information sources is provided at the end of this document.

WHO does not advise the implementation of special screening at points of entry with regard to this event, nor does it recommend that any travel or trade restrictions be applied.

### *Epidemiological and laboratory surveillance*

Detailed surveillance guidance will be published by WHO in the near future. In the interim, Member States should consider the possibility of human infection with A(H7N9) in the following situations:

- any case of severe acute respiratory infection (SARI) in a patient that has travelled to an area with confirmed avian influenza A(H7N9) in the last 7 days or has been in contact with a confirmed case of avian influenza A(H7N9) during that time;
- detection of a SARI cluster with unexplained etiology; or
- any case of SARI detected in health care staff working in settings where SARI patients are being cared for.

In any of the above situations, clinical samples should be taken and analysed within the capacity of the national laboratory system. **All specimens that cannot be subtyped for influenza A and those with inconclusive or unexpected subtyping results should be forwarded, immediately, to the WHO Collaborating Centre (WHO**

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<sup>5</sup> WHO risk assessment: Human infections with influenza A(H7N9) virus as of 13 April 2013 [web site]. Geneva, Switzerland, World Health Organization, ([http://www.who.int/influenza/human\\_animal\\_interface/influenza\\_h7n9/RiskAssessment\\_H7N9\\_13Apr13.pdf](http://www.who.int/influenza/human_animal_interface/influenza_h7n9/RiskAssessment_H7N9_13Apr13.pdf), accessed 22 April 2013).

**CC) for Reference and Research on Influenza, at the National Institute of Medical Research, London, United Kingdom for additional testing.<sup>6</sup>**

The investigation should include complete epidemiological and clinical information, for example: clinical signs and symptoms, date of onset of symptoms, underlying clinical conditions, history of influenza vaccination, history of treatment with oseltamivir or zanamivir, contact with animals, and history of travel, among others.

Guidance for establishing real-time RT-PCR assays for the detection of avian influenza A(H7N9) virus by National Influenza Centres (NICs) in the WHO European Region has been developed by WHO Regional Office for Europe in collaboration with ECDC and the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL) and has been distributed to NICs<sup>7</sup>. Protocols for real-time RT-PCR were published by WHO on 8 April 2013 on the Global Influenza Programme website.<sup>8</sup> NICs could request the avian influenza A(H7N9) virus control material to validate their assays from the WHO CC, following the mechanism described in the Pandemic Influenza Preparedness (PIP) Framework<sup>9</sup>. WHO CC for Surveillance, Epidemiology and Control of Influenza, at the Centers for Disease Control and Prevention, Atlanta, the United States of America has developed a new H7 Real-Time RT-PCR diagnostic kit which is available free of charge to all NICs and can be ordered from the Influenza Reagent Resource<sup>10</sup>.

*Information for the public*

Although there is no evidence of ongoing human-to-human transmission, it is important to implement the following measures to prevent transmission of respiratory viruses:

- Washing hands to reduce transmission.
- Use of “respiratory etiquette” to help prevent transmission of the virus.
- Individuals with flu-like symptoms should avoid leaving their homes to go to work or to other public places and seek medical advice if their condition worsens.

Preventive and control measures in the community should be disseminated in multiple languages to reach all population groups.

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<sup>6</sup> WHO Collaborating Centres for influenza and Essential Regulatory Laboratories [web site]. Geneva, Switzerland, World Health Organization, ([www.who.int/influenza/gisrs\\_laboratory/collaborating\\_centres/list/en/](http://www.who.int/influenza/gisrs_laboratory/collaborating_centres/list/en/)), accessed 22 April 2013).

<sup>7</sup> Technical Briefing note: Diagnostic preparedness in Europe for detection of avian influenza A(H7N9) viruses [web site]. Stockholm, Sweden, European Centre for Disease Prevention and Control (ECDC) (<http://ecdc.europa.eu/en/publications/publications/avian-influenza-h7n9-microbiology-diagnostic-preparedness-for-detection.pdf>), accessed 25 April 2013).

<sup>8</sup> Real-time RT-PCR Protocol for the Detection of Avian Influenza A(H7N9) Virus [web site]. Geneva, Switzerland, World Health Organization, ([http://www.who.int/influenza/gisrs\\_laboratory/a\\_h7n9/en/](http://www.who.int/influenza/gisrs_laboratory/a_h7n9/en/)), accessed 22 April 2013).

<sup>9</sup> Pandemic Influenza Preparedness (PIP) Framework [web site]. Geneva, World Health Organization, ([http://www.who.int/influenza/resources/pip\\_framework/en/](http://www.who.int/influenza/resources/pip_framework/en/)), accessed 08 May 2013).

<sup>10</sup> CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay (EUA) (Catalog No. FluEUA-01), FR-1240. Influenza Reagent Resource, Influenza Division, WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza, Centers for Disease Control and Prevention, Atlanta, the United States of America (<http://www.influenzareagentresource.org/>) accessed 08 May 2013).

## 4) Key references and guidance

WHO/Europe and other international organizations provide information about this event through the web sites listed below. WHO/Europe is working to make key documents available in Russian. As documents become available in Russian, they will be listed in this update. IHR National Focal Points will continue to receive information through the Event Information Site (EIS).

- WHO headquarters  
[www.who.int/influenza/human\\_animal\\_interface/influenza\\_h7n9/en/index.html](http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/index.html)
- WHO Regional Office for Europe  
[www.euro.who.int/A\(H7N9\)](http://www.euro.who.int/A(H7N9))
- European Centre for Disease Prevention and Control  
[http://ecdc.europa.eu/en/healthtopics/avian\\_influenza/Pages/index.aspx](http://ecdc.europa.eu/en/healthtopics/avian_influenza/Pages/index.aspx)