UPDATED RAPID RISK ASSESSMENT

Severe respiratory disease associated with a novel type A influenza virus, A(H7N9) – China

12 April 2013

Main conclusions and recommendations

Background

On 31 March 2013, Chinese authorities announced the identification of a novel reassortant A(H7N9) influenza virus isolated from three unlinked cases of severe respiratory disease in eastern China; two in Shanghai and one in Anhui province. The type A influenza viruses initially isolated from the three cases could not be subtyped and had therefore been sent to the WHO Collaborating Centre for Reference and Research on Influenza at the Chinese Center for Disease Control and Prevention (CDC) where they were sequenced and found to be almost identical and considered to be of avian origin. This is the first time that human infection with avian influenza virus A(H7N9) has been identified.

Since then, human cases have continued to be reported from eastern China, and as of 11 April, there were 38 laboratory-confirmed cases including ten deaths reported from four bordering provinces in eastern China with a concentration of cases in and around Shanghai. Cases occur sporadically, without obvious epidemiological links and there is currently no confirmed human-to-human transmission. Tracing and monitoring of more than 700 contacts have not detected any additional laboratory-confirmed cases. Genetically almost identical viruses have been isolated from poultry live-animal markets. The working hypothesis is that the outbreak is caused by a reassortant avian influenza virus with low pathogenicity for birds, low transmissibility from birds to humans but causing severe disease in infected people. It is assumed that the virus has been introduced to poultry by wild birds but the precise derivation and timeline of events is uncertain and appears widely distributed across eastern China.

Major developments since the first ECDC Rapid Risk Assessment of 3 April 2013

- Genetically closely related avian influenza A(H7N9) viruses have been isolated from healthy chickens, pigeons, ducks, and from environmental samples. Sequences from viruses isolated from a chicken, a pigeon and environmental samples have been posted on GISAID.
- Sporadic human cases have continued to occur without clear epidemiological links.
- The geographical distribution of reported cases has increased in the four affected provinces in eastern China.
- No new clusters have been reported and no cases have been detected among the more than 700 contacts of confirmed cases that have been followed up.
- Three confirmed cases are reported to have had mild disease.
- Biological markers suggestive of mammalian host adaptation have not translated into changes in the way the disease is spreading.
- No human or animal cases have been detected outside of China.

Main conclusions and recommendations, continued

Threat assessment

Such severe disease involving a novel reassortant avian influenza virus is a significant public health event requiring notification under the terms of the International Health Regulations (IHR). As such it was notified through the IHR system by the Chinese authorities. The risk of the disease spreading to Europe via humans in the near future is considered low at this time. However, it is likely that people presenting with severe respiratory infection in the EU and a history of potential exposure in the outbreak area will require investigation in Europe. It is not unlikely that, in the future, there will be laboratory-confirmed cases in the EU who have acquired the infection in China or other yet unrecognised affected areas.

The risk of A(H7N9) virus being transported to Europe in viraemic poultry is low. EU regulations do not permit the importation of live poultry, their day-old chicks and hatching eggs and birds other than poultry (captive birds such as parrots, finches and ornamental birds) from China. The risk of the A(H7N9) virus arriving in Europe with migratory birds cannot be quantified at this time.

There is no epidemiological evidence to date that avian influenza can be transmitted to humans through consumption of food, notably poultry meat and eggs.

Recommendations for the EU/EEA

- EU/EEA citizens working in or visiting China should avoid visiting live bird and animal markets ('wet markets') because of the potential presence of avian influenza viruses that are pathogenic to humans in these markets. They should also avoid direct contact with bird and animal faeces, untreated bird feathers and other animal and bird waste, and they should follow basic hand hygiene rules, e.g. hand-washing with soap and the use of alcohol-based hand rubs.
- Specific food safety recommendations for the EU are not required for the A(H7N9) outbreak. Longstanding advice that chicken and eggs should be properly cooked remains relevant.
- As there is no evidence of human-to-human transmission at this stage, tracing contacts of passengers that are symptomatic during a flight and providing chemoprophylaxis for them is not recommended, but could be considered if the case is later confirmed.
- Public health authorities should continue to apply their national case-finding strategies developed for the A(H5N1) epidemic.
- National public health authorities and infection control managers should alert and remind clinicians and healthcare workers of standard guidance for infection control and contact tracing around cases of severe acute respiratory infections.
- Public health authorities should investigate all clusters of severe respiratory infections and infections in healthcare workers who have been caring for patients with severe acute respiratory disease.
- A(H7N9)-specific deferral criteria or screening tests are not recommended for blood safety.
- In the event of cases being confirmed in the EU/EEA Member States, active tracing and follow-up of their close contacts and of people who may have shared the same exposure should be considered, as well as antiviral prophylaxis.
- Diagnostic and reference laboratories in the EU should continue to use their current generic RT-PCR assays for influenza A for screening and testing of possible cases, if those tests are based on highly conserved internal gene sequences (e.g. in the M-gene segment). The match of primers and probes to the published sequences of the A(H7N9) virus should be checked.
- Clinicians and laboratory specialists should be reminded to consider the possibility of animal influenza infection in persons with severe acute respiratory disease who have, in the previous 10 days, been in China and other countries with circulating animal influenza viruses pathogenic to humans.
- Influenza A virus isolates that cannot be subtyped at national reference laboratories should be sent rapidly to the WHO Collaborating Centre for Reference and Research on Influenza based in Europe.
- Members States should not report cases under investigation for A(H7N9) internationally before confirmation. Clinicians and laboratories should notify national authorities about cases under investigation in accordance with national guidelines.
- Any confirmed case being diagnosed in the EU/EEA area should be reported to international authorities, through the Early Warning and Response System (EWRS) and to WHO under the International Health Regulations (2005). Reporting through EWRS qualifies as IHR notification and avoids double reporting.
- The EU and EU Member States should not implement travel or trade restrictions for countries with A(H7N9) transmission.
- ECDC will develop A(H7N9) case definitions for surveillance and reporting purposes in close consultation with Member States.

Source and date of request

Planned revision by ECDC, 8 April 2013.

Public health issue

The aim of this document is to assess the risk associated with the outbreak of avian influenza A(H7N9) to public health in the EU and to EU citizens, based on the information available.

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ECDC acknowledges the valuable contributions from the above-mentioned experts and institutions. All experts have signed a Declaration of Interest. Opinions expressed by individual experts do not necessarily represent the opinion of their institutions.

This analysis would not have been possible without the virological and molecular data made available in the GISAID database [1] by the WHO Collaborating Centre for Reference and Research on Influenza at the Chinese Center for Disease Control and Prevention, the Harbin Veterinary Research Institute, Ministry of Agriculture, China, and the Hangzhou Center for Disease Control and Prevention, Mingshi, Hangzhou, China.

Event background information

On 31 March 2013, the Chinese Authorities announced the identification of a novel influenza (H7N9) virus infection in three seriously ill people; all three subsequently died. These cases occurred in the Chinese provinces of Shanghai and Anhui. Details for the first three cases are available in the initial Rapid Risk Assessment of 3 April 2013 [2].

Subsequently, sporadic cases occurred in Shanghai and Anhui, as well as in the two neighbouring provinces of Jiangsu and Zhejiang. As of 11 April, 38 cases of human infection with influenza A(H7N9) have been confirmed; Shanghai (18), Jiangsu (12), Zhejiang (6), Anhui (2). Details of all confirmed cases are available in the most recent epidemiological update [3].

The date of onset ranges from 19 February to 4 April. Thirty-five of the confirmed cases have severe disease and ten of the cases (26%) have died. Only three are considered to be mild cases. There is only one child case, a 4-year-old boy who has recovered from a mild disease. The age of the cases ranges from 4 to 87 years with a median age of 65 years.

No epidemiological links have been identified between the cases. Over 700 close contacts have been followed-up and only three are reported to have developed symptoms, as part of two potential small family clusters. In Shanghai, two family members of the first confirmed case were admitted to a hospital with pneumonia. One recovered and the other died later in February from respiratory failure. The cause of their illnesses has not yet been determined. In Jiangsu, an investigation is on-going into a family contact who developed symptoms. Up to now, none of the over 700 close contacts investigated has been found positive on PCR testing. For 10 of the 38 cases, an exposure to animals (mostly poultry) has been presumed. However, exposure information is not complete for all cases and therefore no conclusions can be drawn from it at this stage.

The Chinese CDC has made available avian influenza A(H7N9)-specific tests. It is reported that these have been distributed to over 400 influenza monitoring sites across the country, major infectious disease hospitals and research agencies.

Animal surveillance is on-going around the cases and the Chinese Ministry of Agriculture notified the World Organization for Animal Health (OIE)[i] about the detection of genetically similar A(H7N9) isolates. The viruses were detected in samples from a pigeon for consumption, chickens, ducks and in environmental samples from agricultural products wholesale markets in Shanghai. A(H7N9) viruses have also been detected in 14 samples from ducks and chickens from five additional live bird markets in Jiangsu, Anhui and Zhejiang. The Ministry of Agriculture also reported that 'stamping-out' control measures have commenced in poultry markets.

Disease background information

Virological information

Initial characterisation of the viruses was carried out by the WHO Collaborating Centres for Reference and Research on Influenza in Beijing, and additional genetic analyses were carried out by the WHO Collaborating Centres in Tokyo and Atlanta. The summary has been published on the WHO website [4]. Detailed genetic sequence data from human, avian and environmental isolates of A(H7N9) viruses have been published on the GISAID website [1].

The outbreak virus is a reassortant avian influenza A virus in which the six RNA segments encoding the internal proteins are closely similar to avian A(H9N2) viruses recently isolated in China. The segment encoding haemagglutinin (HA) comes from a Eurasian A(H7) avian influenza virus and the segment for neuraminidase (NA) is most similar to avian H11N9 and H7N9 viruses. The H7 and N9 gene segments are, however, considerably less close to the nearest known relatives and it is clear that the immediate ancestral viruses that contributed the H7 and the N9 genes remain unknown. This gene constellation makes the outbreak strain different from previously isolated avian influenza A(H7N9) viruses including those reported in birds in Europe. The reservoir for the novel virus infecting humans may or may not be poultry. Genetic markers associated with high pathogenicity in poultry have not been detected but this finding requires further confirmation by intravenous pathogenicity index testing in chickens. High pathogenicity in poultry does not necessarily indicate high pathogenicity in humans. The adaptation of the novel A(H7N9) viruses to mammalian hosts is suggested by mutations known to confer recognition of a receptor (sialic acid linked alpha 2-6 to galactose) present in the upper respiratory tract of humans and other mammals, the deletion of a stalk region of the NA protein frequently observed upon transfer of viruses from wild fowl to poultry or mammals, and a substitution in the PB2 gene that is known to improve the replication of avian influenza viruses in mammals. Further research into the virological characteristics is on-going [5–7].

S31N, a M-gene marker for adamantane resistance, was found in all three human isolates. It is therefore anticipated that the viruses will be resistant to amantadine and rimantadine, two antivirals no longer in use in Europe. The WHO Collaborating Centre for Reference and Research on Influenza in Beijing have confirmed that A(H7N9) is sensitive to oseltamivir and zanamivir in phenotypic tests.

Diagnostics for A(H7N9) in humans

Based on sequence analysis, it is expected that the generic RT-PCR assays for influenza A virus that are based on highly conserved viral gene sequences, e.g. in the M-gene, will detect the novel virus. Diagnostic and reference laboratories in the EU should therefore continue to use their current generic RT-PCR assays for influenza A virus for screening and testing of possible cases, if those tests are based on highly conserved internal gene sequences and have been confirmed *in silico* to fit the M-gene of the A(H7N9) virus. Clinically validated assays that specifically detect A(H7N9) viruses are not yet available in Europe, although a couple of countries with frequent H7 poultry outbreaks have assays available that *in silico* are fit to subtype the A(H7N9) virus. According to a survey conducted in July 2011, many national influenza reference laboratories are using PCR tests that likely detect this novel virus and should therefore be reasonably well prepared [8].

In the diagnostic laboratory assays, the novel viruses should be detected as positive for influenza A virus, and negative for influenza B, A(H1), A(H1)pdm09, A(H3) and A(H5) viruses. Hence, A(H7N9) viruses are expected to be classified as un-subtypeable influenza A. Laboratories with experience of A(H7) subtyping may be able to subtype the novel viruses with their existing H7 primers and probes.

It is standard procedure to send influenza A virus isolates or clinical samples that cannot be subtyped at the national reference laboratory to a WHO Collaborating Centre for Reference and Research on Influenza for characterisation, as was done in China when the first A(H7N9) isolates were sent to the WHO Collaborating Centre

[i] http://www.oie.int/

for Reference and Research on Influenza in Beijing. In Europe, the WHO Collaborating Centre for Reference and Research on Influenza is located at the National Institute for Medical Research (Mill Hill) in London. All EU/EEA Member States are expected to urgently send un-subtypeable A viruses and subtyped A(H7) viruses to the for Collaborating Centre for Reference and Research on Influenza in London for further characterisation.

Vaccines against influenza A(H7N9)

It is unknown whether current H7 candidate vaccine viruses are cross-protective and candidate vaccine viruses based on the A(H7N9) virus will be developed [4].

Influenza candidate vaccine strains are normally developed in WHO collaborating laboratories, WHO Essential Regulatory Laboratories or research laboratories, and then shared with all vaccine manufacturers. The WHO collaborating laboratories for Europe are the WHO Essential Regulatory Laboratory National Institute for Biological Standards and Control (NIBSC) and the WHO Collaborating Centre Collaborating Centre for Reference and Research on Influenza at the National Institute for Medical Research (NIMR), both in the UK. The Chinese CDC, WHO, US CDC, BARDA and NIBSC, among others, are facilitating development of a potential candidate vaccine virus for the influenza A(H7N9) strain in preparation for possible future vaccine development. The initial approach is using synthetic biology techniques utilising the published genetic sequences of the new virus. These techniques are available in the WHO Collaborating Centers, a number of research laboratories and some vaccine manufacturers. In addition, the cultivated A(H7N9) virus strain has been shared by China with the US CDC. In Europe, NIBSC as the WHO Essential Regulatory Laboratory and the WHO Collaborating Centre Collaborating Centre for Reference and Research on Influenza at NIMR, London, UK, will receive the new virus. Influenza candidate vaccine virus strains intended for vaccine production are usually developed in a few laboratories working with the WHO GISRS (Global Influenza Surveillance and Response System) and then shared with all vaccine manufacturers.

Contracts between the US government and vaccine manufacturers ensure that vaccine candidate vaccine virus strains developed either by researchers or manufacturers are open-source and can be freely shared with all stakeholders. In a media briefing by US CDC last Friday, 5 April 2013, the US efforts for development of a candidate vaccine strain were presented [9].

Human and animal surveillance

Surveillance for severe respiratory infections in humans

Human case-finding for the novel reassortant influenza A(H7N9) virus is similar to the one developed for influenza A(H5N1). Persons with severe acute respiratory disease who have recently been in countries[ii] with on-going transmission of animal influenza viruses that are pathogenic for people, should be tested. Also, any clusters of severe respiratory infection, regardless of travel history, and severe infections among healthcare workers who have cared for patients with severe acute respiratory disease need to be thoroughly investigated. It is critical that isolates of un-subtypeable influenza A viruses are rapidly sent to the WHO Collaborating Centre for Reference and Research on Influenza in London.

The US Centers of Disease Control and Prevention have published interim guidance, including a case definition [10].

Surveillance and control of low and high pathogenic influenza in poultry and other captive birds in the EU

EU animal health legislation [11] requires the control of outbreaks in poultry and other captive birds of highly pathogenic and low pathogenic avian influenza viruses of the H5 and H7 subtypes. Suspected and confirmed presence of infection in poultry and other birds must be immediately notified to the competent animal health authority. EU Member States must carry out surveillance programmes in poultry and wild birds [12] in order to detect the circulation of avian influenza viruses according to harmonised guidelines [13].

The EU Reference Laboratory in Weybridge for avian influenza, networking with the National Reference Laboratories for avian influenza in Member States, has confirmed the predicted utility of EU recommended PCR protocols for the detection of the H7N9 virus (both H7 and M gene assays) based on sequence comparison in birds. An empirical assessment will be carried out once the virus is available.

EU legislation regarding the import of live poultry from China

Importation to the EU of live poultry, their day-old chicks and hatching eggs, and birds other than poultry (captive birds such as parrots, finches and ornamental birds) from China is not authorised [14].

[ii] Countries recently (2012 and 2013) reporting A(H5N1) human cases are Bangladesh, China, Cambodia, Egypt, Indonesia, Laos and Vietnam http://www.who.int/influenza/human_animal_interface/EN_GIP_20130312CumulativeNumberH5N1cases.pdf

Epidemiological characteristics

At this stage of the investigations in China, the data are not complete enough to fully understand the nature of the animal reservoir, how poultry become infected, the routes of transmission, the potential for human-to-human transmission, the incubation period and the risk factors for infection. The reservoir and routes of transmission to humans are under investigation by the Chinese authorities. The detection of A(H7N9) virus in samples from pigeons, chickens, ducks and environmental specimens at eight markets in all four provinces indicates that poultry, or other birds, might play an important role in transmission to humans. While a proportion of the cases have mentioned exposure to poultry, it should be kept in mind that it is common to buy live poultry for domestic consumption in China. Other possible animal reservoirs remain to be investigated. There is no information available about analytical studies of risk factors.

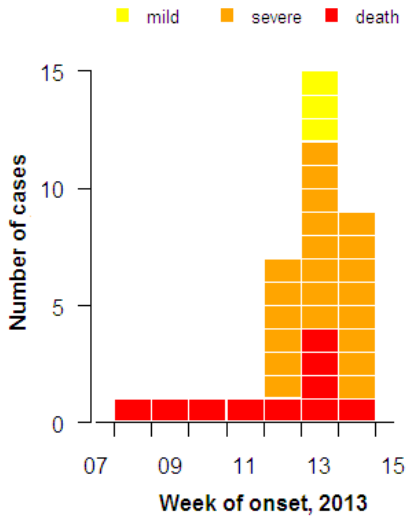
The cases are widely distributed in mid-eastern China and over the last week the affected area has been expanding. One recent case was reported from a city 600 km north-west of Shanghai. This suggests that the virus is widely distributed in its animal reservoir. Poultry density is very high in this part of China and the extensive poultry trade might contribute to distribution of the virus.

There is no convincing evidence for human-to-human transmission at this stage of the outbreak. Chinese authorities have followed-up more than 700 close contacts and taken samples for RT-PCR from many of them without detecting infections. There is on-going investigation into a few symptomatic cases among close contacts, but they have not so far been laboratory-confirmed to have A(H7N9) infections. If the two small potential family clusters under investigation were to be confirmed A(H7N9) infections, it would remain to be determined if they resulted from human-to-human transmission or from a common exposure to an animal or environmental source.

Though the virus appears to cause no or mild disease in poultry, it seems to be highly pathogenic to humans. The case-fatality rate has so far been 26% and most cases had severe disease. However, the reporting of the first three mild cases suggests that the clinical spectrum may be wider than initially presumed. Human influenza surveillance in China is currently based on severe acute respiratory infections (SARI). Broader surveillance could detect more mild cases which currently remain undiagnosed. The median age of the cases is high, at 65 years, with a large proportion being retired, and only one child has so far been found to be infected. That higher age is a risk factor could be explained by higher exposure to poultry in this age group, but this needs to be explored further. There do not seem to be notable clinical risk factors so far, but information remains incomplete. Dates of disease onset are from 19 February to 4 April. It is unclear how well the reported cases reflect the true epidemiology or rather reflect the availability of the test (case ascertainment bias). Future serosurveys, yet to be developed, might shed a better light on the zoonotic and human-to-human transmissibility.

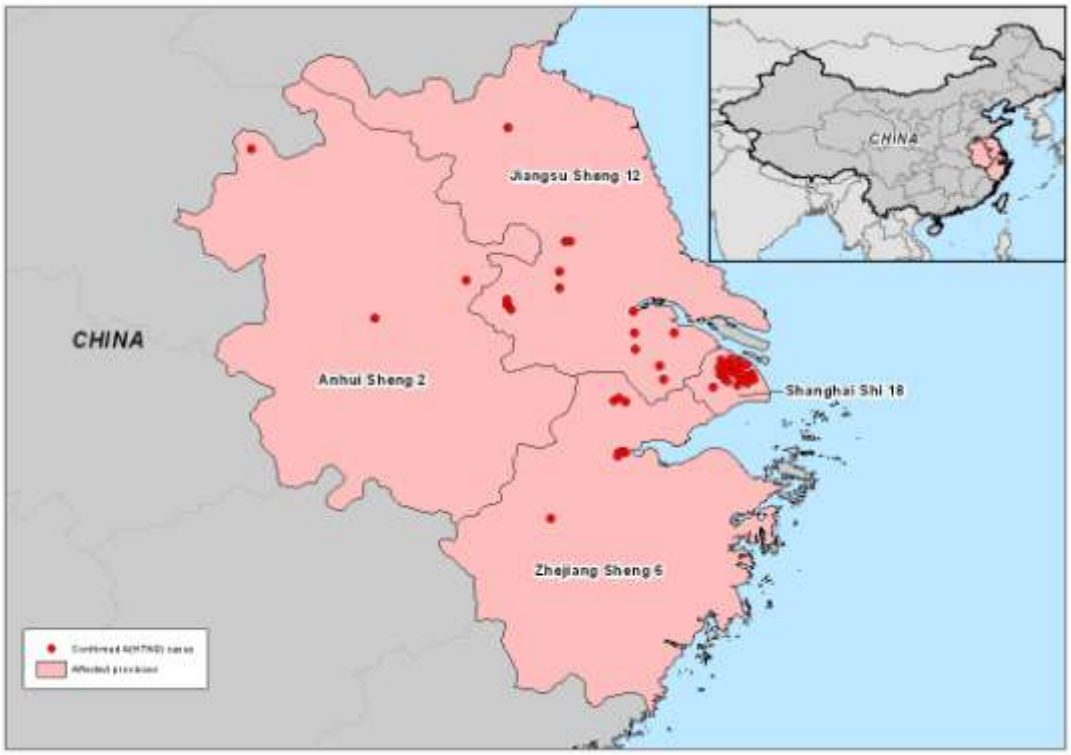
The strong influenza surveillance system in China is not reporting an overall increase in influenza virus detection or atypical pneumonia cases in the most recent reporting period, although even this is hard to interpret at a time when rates of influenza virus transmission are expected to be falling. However, transmission would have to be advanced for those systems to show a signal.

Figure 1. Distribution of avian influenza A(H7N9) human cases by week of onset of symptoms, China, as of 11 April 2013 (n=35) *



** Note: as of 11 April, three cases have unknown date of onset and are not included in the graph.*

Figure 2. Distribution of cumulative number of avian influenza A(H7N9) human cases by province, China, 19 February – 11 April 2013 (n=38)



Discussion

Previous A(H7) infections in humans have tended to be mild [15–17]. The exception is one death during a large outbreak in poultry in the Netherlands involving highly pathogenic avian influenza A(H7N7) virus [18,19]. The death in the Dutch case was associated with an E627K substitution in PB2 of the H7 influenza virus [18]. The same E627K substitution has been associated with high virulence, host range adaptation and airborne transmission in H5 viruses though the significance of its presence here is yet to be clarified [20–22]. It may be significant that the three A(H7N9) viruses isolated from humans also have this E627K substitution. Whether this substitution has the same effect in the A(H7N9) virus as in the H5 and H7 viruses is unknown at present. The absence of the PB2 E627K substitution in the non-human isolates may indicate either that the change occurs in the infected individuals, or that another subset of the virus that has not yet been sequenced, is circulating in animals and causing infections in humans. Further, there is reason for concern over human infections with A(H7) viruses in general [23]. This is an A(H7N9)-A(H9N2) reassortant, and laboratory studies of A(H9N2) viruses with animals have suggested that those viruses have pandemic potential [24]. Low pathogenic avian influenza A(H9N2) virus infections of humans have usually resulted in uncomplicated influenza illness, but one case of lower respiratory tract disease in an immunocompromised adult has been reported [25].

In the most likely scenario, the novel reassortant A(H7N9) virus causes mild or no disease in birds but is transmissible among birds, and is spreading among the poultry populations in eastern China. People are occasionally infected through exposure to infected poultry or contaminated environment, and possibly other infected animals. The outbreak was detected because the virus causes severe disease in at least a proportion of infected persons. The current absence of confirmed clusters of cases and the fact that no infections have been detected by PCR among the contacts of confirmed cases, indicates no or very limited occurrence of human-to-human transmission.

Recent reports of three confirmed cases with mild symptoms may indicate a wider spectrum of disease. If mild or asymptomatic human infections occur, this could indicate a wider spread of the virus. This scenario would have to be validated by serological studies and continued contact tracing. The currently available epidemiology suggests a higher zoonotic (animal-to-human) transmissibility for A(H7N9) viruses than for A(H5N1) viruses [26]. It is yet unknown whether the source of the human infections is poultry. Several species of poultry and other birds are sold in the live animal markets in China, and once introduced, the virus is likely to spread across species and contaminate the environment. Detection of the virus in one species of bird does not necessarily mean that this species is responsible for transmission to humans.

Detection of low pathogenic avian influenza viruses is not universally required. The extent to which influenza A(H7N9) virus has spread in poultry in China and other countries remains unknown.

ECDC threat assessment for the EU

The emergence of a novel reassortant avian influenza virus capable of causing severe disease in humans is a significant public health development. The rapid notification by Chinese authorities under the International Health Regulations, and the continued communication of the findings of outbreak investigations has facilitated the assessment of the risk to human health from this outbreak. Thirty-eight laboratory-confirmed cases of A(H7N9) infection have been reported from four eastern provinces in China. Twenty-five cases presented with severe disease, of which ten have died. This is the first time that human infection with influenza A(H7N9) virus has been identified and the first time that human infection with a low pathogenic avian influenza A virus has been associated with a fatal outcome.

The risk of the disease spreading to Europe via humans in the near future is considered low at this time. However, it is likely that people presenting with severe respiratory infection in the EU and a history of potential exposure in the outbreak area will require investigation in Europe. It is not unlikely that, in the future, there will be laboratory-confirmed cases in the EU who have acquired the infection in China or other yet unrecognised affected areas.

There is insufficient evidence to quantify the risk of A(H7N9) developing into a virus that transmits from human to human. Close monitoring of the outbreak epidemiology and the viruses' genetic variation over time will be critical for assessing this risk.

The risk of healthcare-associated transmission when caring for A(H7N9) infected patients cannot yet be quantified, but close patient care and diagnostic procedures have been shown to increase the risk of transmission of other viruses that do not normally transmit from person to person. The infective period for A(H7N9) cases is not known but patients admitted with A(H7N9) infection are likely to be viraemic and to excrete the virus in body fluids [27].

The risk of A(H7N9) virus being transported to Europe in viraemic poultry is low. EU regulations do not permit the importation of live poultry, their day-old chicks and hatching eggs and birds other than poultry (captive birds such as parrots, finches and ornamental birds) from China. The only poultry commodities authorised for import from China into the EU are heat-treated poultry meat, from the only province of Shandong, and egg-products that have also been heat-treated. Given the very heat-labile nature of all influenza viruses, these commodities are not considered to pose any risk of any influenza virus transmission to consumers.

The risk of the A(H7N9) virus arriving in Europe with migratory birds cannot be quantified at this time. The European Food Safety Authority (EFSA) has performed three risk assessments in the past regarding avian influenza that would to a large extent also cover pathways for A(H7N9) [28–30]. The hypothesis that poultry in the affected area have been infected by wild birds has not been confirmed. The virus has so far not been detected in wild birds and the geographic distribution of infected poultry remains to be established. The A(H5N1) virus has been detected in bird populations in Asia, Africa and Europe on several occasions.

There is no epidemiological evidence to date that avian influenza can be transmitted to humans through the consumption of food, notably poultry meat and eggs.

There is no specific guidance on blood or tissue donor deferral for exposure to avian influenza. The incubation period for A(H7N9) is unknown but assumed to be short, and there is no reason to believe that infected people will be viraemic beyond the acute disease episode. Therefore, the risk of transmission through blood transfusion can be considered very low in the context of the current donor selection procedures.

Recommendations for the EU/EEA

- EU/EEA citizens working in or visiting China should avoid visiting live bird and animal markets ('wet markets') because of the potential presence of avian influenza viruses that are pathogenic to humans in these markets. They should also avoid direct contact with bird and animal faeces, untreated bird feathers and other animal and bird waste, and they should follow basic hand hygiene rules, e.g. hand-washing with soap and the use of alcohol-based hand rubs [31–34].
- Specific food safety recommendations for the EU are not required for the A(H7N9) outbreak. Longstanding advice that chicken and eggs should be properly cooked remains relevant [35,36].
- As there is no evidence of human-to-human transmission at this stage, tracing contacts of passengers that are symptomatic during a flight and providing chemoprophylaxis for them is not recommended, but could be considered if the case is later confirmed [31].
- Public health authorities should continue to apply their national case-finding strategies developed for the A(H5N1) epidemic.
- National public health authorities and infection control managers should alert and remind clinicians and healthcare workers of standard guidance for infection control and contact tracing around cases of severe acute respiratory infections [37,38].
- Public health authorities should investigate all clusters of severe respiratory infections and infections in healthcare workers who have been caring for patients with severe acute respiratory disease.
- A(H7N9)-specific deferral criteria or screening tests are not recommended for blood safety.
- In the event of cases being confirmed in the EU/EEA Member States, active tracing and follow-up of their close

contacts and of people who may have shared the same exposure should be considered, as well as antiviral prophylaxis.

- Diagnostic and reference laboratories in the EU should continue to use their current generic RT-PCR assays for influenza A for screening and testing of possible cases, if those tests are based on highly conserved internal gene sequences (e.g. in the M-gene segment). The match of primers and probes to the published sequences of the A(H7N9) virus should be checked.
- Clinicians and laboratory specialists should be reminded to consider the possibility of animal influenza infection in persons with severe acute respiratory disease who have, in the previous 10 days, been in China and other countries with circulating animal influenza viruses pathogenic to humans[i].
- Influenza A virus isolates that cannot be subtyped at national reference laboratories should be sent rapidly to the WHO Collaborating Centre for Reference and Research on Influenza based in Europe.
- Members States should not report cases under investigation for A(H7N9) internationally before confirmation. Clinicians and laboratories should notify national authorities about cases under investigation in accordance with national guidelines.
- Any confirmed case being diagnosed in the EU/EEA area should be reported to international authorities through the Early Warning and Response System (EWRS) and to WHO under the International Health Regulations (2005). Reporting through EWRS qualifies as IHR notification and avoids double reporting.
- The EU and EU Member States should not implement travel or trade restrictions for countries with A(H7N9) transmission.
- ECDC will develop A(H7N9) case definitions for surveillance and reporting purposes in close consultation with Member States.

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