RAPID RISK ASSESSMENT

Human infection with avian influenza A(H7N9) virus

Fifth update, 27 January 2017

Conclusions and options for response

Since the notification of a novel reassortant influenza A(H7N9) virus on 31 March 2013, a total of 1 033 laboratory-confirmed cases of human infection with avian influenza A(H7N9) virus have been reported. This is the fifth winter season in the northern hemisphere with human cases caused by A(H7N9) infections. During this wave, the number of human cases is already higher than during the whole of the last wave in 2015–16. Disease numbers are significantly higher than during the same periods in 2014–15 and 2015–16. A steep increase in human cases has been reported since the beginning of December 2016 from China. The epidemiology, however, does not seem to have changed during the current wave of infections. The majority of recently reported human cases are associated with exposure to infected live poultry or contaminated environments, including markets where live poultry are sold. The age distribution of the cases is comparable with previous waves. Influenza A(H7N9) viruses continue to be detected in poultry (and their immediate environment) in the areas where human cases are occurring, but more human cases are being detected in rural areas. The upsurge in human cases is most likely due to increased environmental contamination, mostly related to live bird markets.

At present, the most immediate threat to EU citizens is to those living or visiting influenza A(H7N9)-affected areas in China. It is advisable to avoid live bird markets or backyard farms as well as contact with live poultry or their droppings. Food should be only consumed if properly cooked. The environmental contamination and the related higher risk of exposure to A(H7N9) points towards the possibility of travel-related cases, especially in relation to Chinese New Year on 28 January. The recent upsurge of human cases due to a higher risk of exposure indicates the possibility that cases will be imported to Europe. However, the risk of the disease spreading among humans within Europe is still considered low as the virus does not appear to transmit easily from human to human: investigations do not support sustained human-to-human transmission.

Caution should be taken by people travelling to China to avoid direct exposure to poultry, live poultry markets or backyard farms. Travellers who have visited affected areas and develop respiratory symptoms and/or fever within 10 days of their return should consult a physician and inform him/her about their recent travel history to facilitate early diagnosis and treatment. People in the EU presenting with severe respiratory or influenza-like infection and a history of travel to the affected areas in China – with potential exposure to poultry or live bird markets – will require careful investigation, management and infection control. Adequate samples for influenza tests should be rapidly taken and processed from patients with relevant exposure history within 10 days of symptom onset. Early or presumptive treatment with neuraminidase inhibitors should be considered for suspect or confirmed cases, in line with relevant national and international recommendations. Contacts of confirmed cases should be followed up and tested. Post-exposure prophylaxis should be considered.

Sporadic cases imported from China do not alter ECDC's risk assessment from February 2015.

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Source and date of request

Internal ECDC decision on 20 January 2017 due to the large increase in human infections with avian influenza A(H7N9) virus in China, September 2016 – January 2017.

Public health issue

This document aims to:

- summarise the epidemiological and virological information on human infections with avian influenza A(H7N9) viruses following an upsurge in cases since December 2016 in China; and
- assess the risk to public health in the EU/EEA and to EU/EEA citizens.

This rapid risk assessment builds on earlier ECDC rapid risk assessments on avian influenza.

Consulted experts

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External experts from the following institutions contributed to this risk assessment: WHO Regional Office for Europe and WHO Headquarters, Geneva

ECDC acknowledges the valuable contributions of all experts. All experts have submitted Declarations of Interest. ECDC has reviewed these and finds that none of them represent conflicts of interest with the comments and suggestions the experts have made. It should be noted that opinions expressed by individual experts do not necessarily represent the opinion of their institutions.

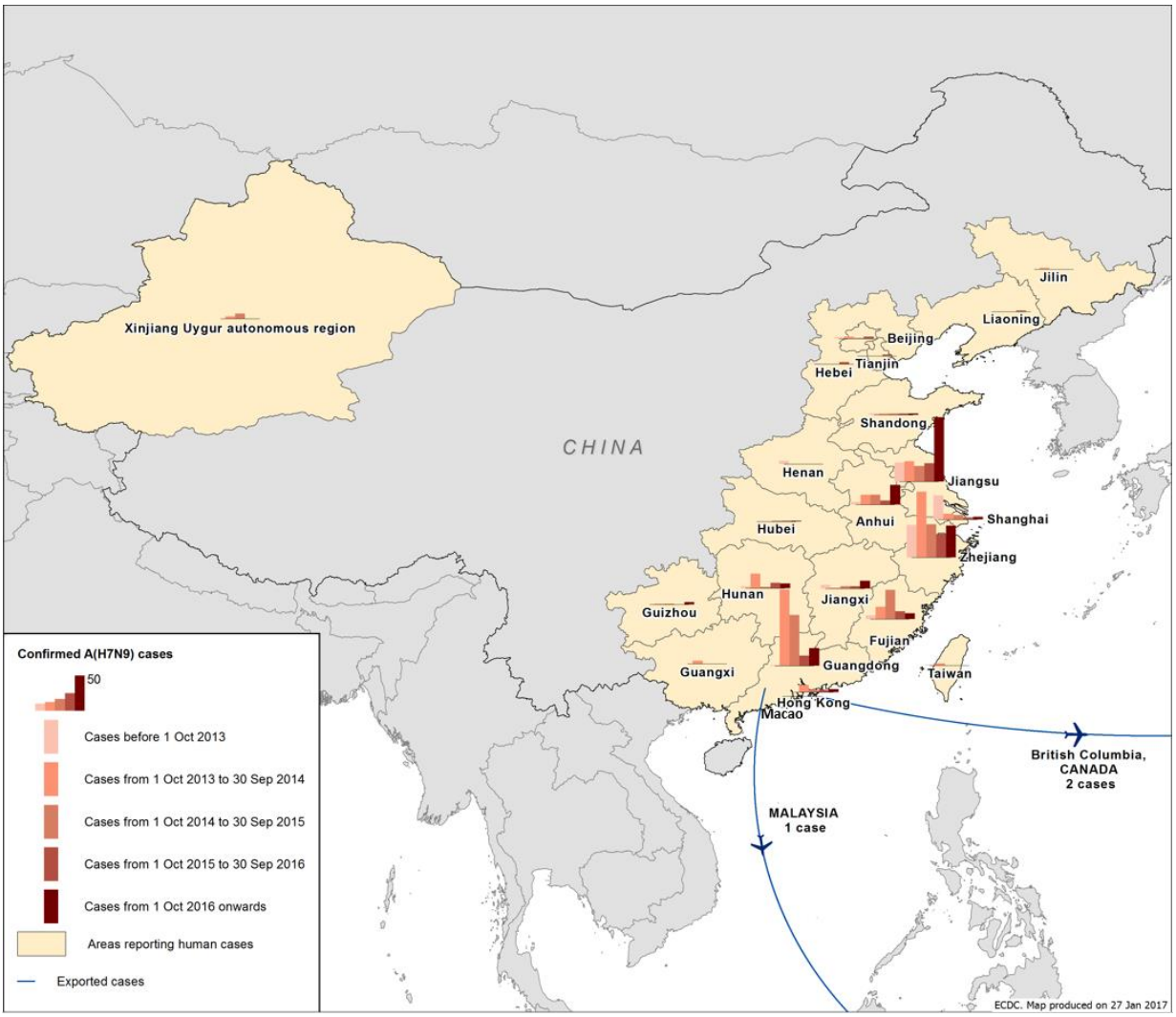
Event information

China

In March 2013, Chinese authorities announced the identification of a novel reassortant A(H7N9) influenza virus in patients in eastern China. According to WHO, as of 18 January 2017, 918 laboratory-confirmed cases have been reported in China or have had a recent travel history to China prior to disease onset [1]. On 24 January 2017, the health authorities in Hong Kong reported that since March 2013 (as of 23 January 2017) a total of 1 033 human cases of avian influenza A(H7N9) have been reported globally; since November 2016, 229 cases have occurred in mainland China and 235 overall [2] (Figure 1).

So far, the majority of cases have been reported during the winter months December to April (Figure 2). Apart from a locally acquired infection of an asymptomatic case with exposure to infected poultry in Macau, all cases occurred in mainland China. The 28 cases detected in other areas outside mainland China were travel-related and acquired the infection during their stay in mainland China [2,3]. In mainland China, the provinces with the greatest number of reported cases included Zhejiang (26%), Guangdong (22%) and Jiangsu (19%). During the current fifth wave, Jiangsu province has reported most of the cases (91/235; 39%) (Figure 1 and Table 1). Hong Kong reported four imported cases from Guangdong province. Two cases were detected in Macao, one locally acquired and one imported case from mainland China. During the current wave, the human cases have shown a more widespread distribution across the country, indicating a broader risk of exposure within mainland China.

Figure 1. Distribution of confirmed A(H7N9) human cases by place of reporting in China or with recent travel history to China, week 7/2013 to 4/2017



Numbers according to WHO report dated 18 January 2017 [1] and Avian influenza report *of the Centre for Health Protection of the Department of Health, Hong Kong, 24 January 2017 [2]*

Table 1. Number of human cases due to A(H7N9) infection, by region

Region	Cumulative no. of cases since 2013 (N=1 033 cases)	Cumulative no. of cases since November 2016 (N=235 cases)
Zhejiang province	264	45
Guangdong province	221	26
Jiangsu province	195	91
Fujian province	82	8
Anhui province	64	28
Shanghai municipality	55	4
Hunan province	44	10
Jiangxi province	25	11
Shandong province	11	2
Xinjiang Uygur autonomous region	10	-
Beijing municipality	9	-
Guizhou province	5	3
Hebei province	4	-
Henan province	4	-
Guangxi province	3	-
Hubei province	3	1
Jilin province	2	-
Tianjin municipality	2	-

Region	Cumulative no. of cases since 2013 (N=1 033 cases)	Cumulative no. of cases since November 2016 (N=235 cases)
Liaoning province	1	-
Hong Kong	20*	4
Macao	2**	2
Taiwan	4*	-
Canada	2*	-
Malaysia	1*	-

** All cases imported from mainland China ** The latest case imported from mainland China*

Source: Avian influenza report *of the Centre for Health Protection of the Department of Health, Hong Kong (as of 23 January 2017) [2]*

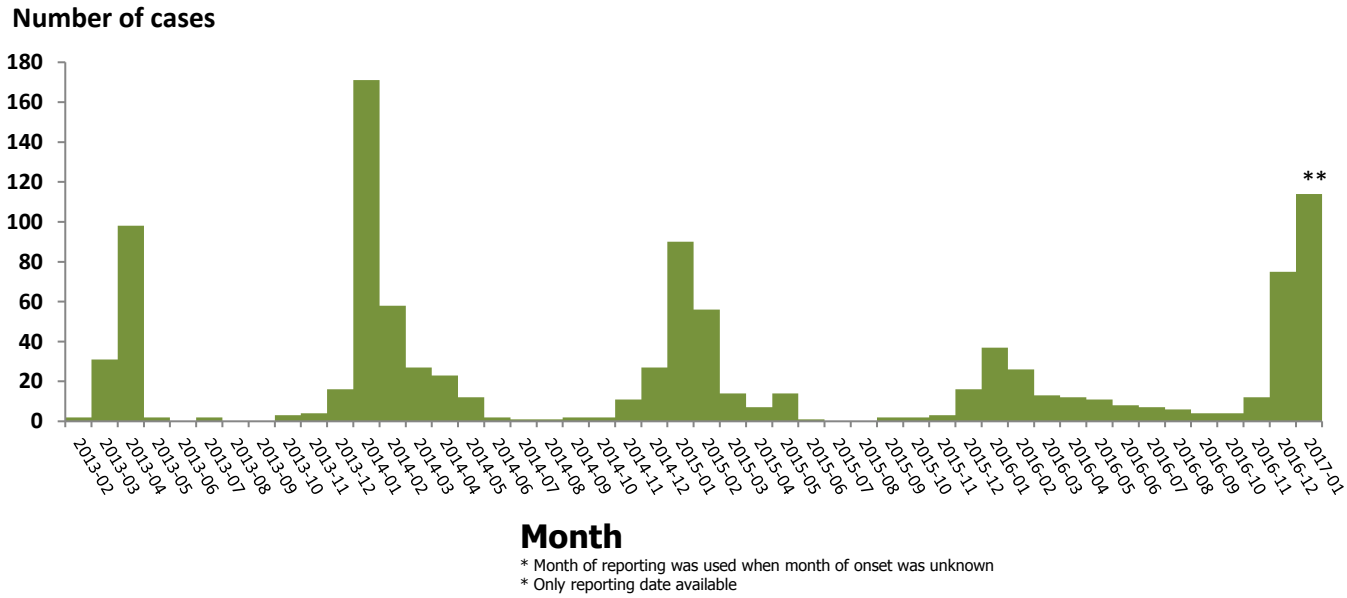
The A(H7N9) outbreak shows a seasonal pattern peaking in the winter months, with only sporadic cases during the summer (Figure 2). Cases reported between week 41 of one year and week 40 of the subsequent year are considered to belong to one epidemic wave. The first wave in spring 2013 (weeks 7/2013–40/2013) included 135 cases; 319 cases were reported during the second wave (weeks 41/2013–40/2014), 223 cases during the third wave (weeks 41/2014–40/2015), and 121 in the fourth wave (weeks 41/2015–40/2016). A fifth wave started in October 2016 (week 41/2016), with 235 cases as of 24 January 2017. The continuing upsurge in cases since December 2016 is comparable with the epidemic curve observed during the second wave. The total number of cases as at 24 January 2017 (week 4) is already higher than the total of the third and fourth waves until week 40 (Figure 2, Table 1).

The first case of the fifth epidemic wave had onset of illness on 28 September 2016 in Zhejiang province [4]. From September to November 2016, a total of eight cases were reported in four provinces (Jiangsu, Zhejiang, Fujian, Guangdong), which is similar to the number of cases during the same period in prior epidemic waves. However, since 1 December 2016, the number of cases has substantially increased, with 106 cases reported in December 2016 alone. As of 31 December 2016, the number of reported cases in the fifth epidemic wave was 11.4, 2.7 and 6.1 times that observed in the corresponding periods during the second (10 cases), third (31 cases) and fourth (16 cases) epidemics, respectively [4].

During the current epidemic wave, the median age was 55 years, with more men (68%) than women being infected, which is comparable with the previous waves. A higher number of infected persons in rural areas and farmers were reported this winter. For those cases, available information referred to exposure history, contact to live poultry, live poultry markets or backyard poultry [3,4].

Two clusters with two cases each were identified and investigated during the current wave. Additional clusters were identified previously, but so far no tertiary transmission has been observed, and human-to-human transmission remains rare [5,6].

Figure 2. Epidemic curve of human infections with A(H7N9) virus by week, February 2013–24 January 2017 (N=1 016)



Numbers according to WHO report dated 18 January 2017 [1] and Avian influenza report *of the Centre for Health Protection of the Department of Health, Hong Kong, 24 January 2017 [2]*

Of 918 cases notified globally at least 359 have died (case-fatality ratio (CFR)=39%). These estimates are based on the information available at the time of notification. Therefore, CFR may be affected by completeness of information on outcome at the time of notification. The CFR ranged between 32% and 44% during the five waves and has not significantly changed throughout (Table 2) [4,7].

Table 2. Number of reported cases* and fatalities due to A(H7N9) infection

	First wave (2/2013–9/2013)	Second wave (10/2013–9/2014)	Third wave (10/2014–9/2015)	Fourth wave (10/2015–10/2016)	Fifth wave (10/2016–1/2017) Three months	Total number of cases (2/2013–1/2017)
Cases	135	319	223	121	120	918
Deaths**	43	134	98	45	39	359
CFR (%)	32%	42%	44%	37%	33%	39%

** Only cases for which outcome data were available were included*

*** Estimates are based on the information available at the time of notification. CFR may be affected by completeness of information about outcome at time of notification.*

Virological information

The novel influenza A(H7N9) viruses are the first low pathogenicity avian viruses that have been documented to cause severe human disease. The diversity of circulating avian influenza viruses in different bird species in China supports reassortment processes and the evolution of new emerging viruses. A(H7N9) is a reassortant avian influenza A virus in which the six RNA segments encoding the internal proteins are closely related to avian A(H9N2) viruses that emerged in the chicken population in China [8-11]. The gene encoding haemagglutinin (HA) belongs to the Eurasian A(H7) avian influenza virus lineage, and the segment for neuraminidase (NA) is most similar to avian A(H11N9) and A(H7N9) viruses. The reservoir for this novel virus remains unknown, although a continuous co-circulation of multiple A(H9N2) genotypes in farmed poultry over a longer time might be responsible for antigenic changes and adaptation to chickens [11]. Evolution processes of A(H7N9) viruses in the poultry population have been ongoing since 2013, resulting in a genetic heterogeneity across different regions in China [12,13]. Genetic characteristics of A(H7N9) viruses are of concern for their pandemic potential because they indicate that these viruses have the ability to bind to human and avian influenza virus receptors, α-2,6- and α-2,3-linked sialic acid residues, respectively, and replicate in the human host [14]. Viruses from infected humans in the fifth wave did not show an altered risk profile compared to viruses from previous waves. The genetic markers for mammal adaptation and antiviral resistance remained similar to those already reported in previous waves [4,7].

Animal infections and environment detection

Active surveillance among animals for A(H7N9) is ongoing in China. Low pathogenic avian influenza virus A(H7N9) is enzootic in the Chinese poultry population, and positive detections have been reported from wild birds, poultry and environmental samples taken from live bird markets in several cities and provinces where human cases have also occurred (e.g. Anhui, Fujian, Guangdong, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Shanghai and Zhejiang) [3]. Additionally, environmental samples are collected at wholesale live bird markets, live bird trading areas at farmers' markets, large-scale poultry farms, village/backyard poultry holdings, poultry slaughterhouses, wild migrating bird habitats, and other locations. The virus has been detected previously in chickens, particularly in the yellow and Silkie chicken breeds, ducks, pigeons, a goose and a tree sparrow, but not in pigs. Judging from surveillance results, chickens appear to be the most affected poultry species [15,16].

Since March 2013, and up to January 2015, the Food and Agriculture Organization of the United Nations (FAO) has collected reports of positive virological samples from birds and the environment. These reports were submitted by the Chinese ministry of agriculture, the Chinese ministry of health, and the Chinese Centre for Disease Control and Prevention and cover the following provinces and areas: Anhui, Fujian, Guangdong, Guangxi, Hebei, Henan, Hong Kong, Hunan, Jiangsu, Jiangxi, Macao, Ningxia Hui autonomous region, Qinghai, Shandong, Shanghai, Xinjiang and Zhejiang. Samples which tested positive for influenza A(H7N9) during 2013–2015 came from the environment, particularly from live poultry markets, but also some backyard farms, a kitchen and a slaughterhouse [17,18]. In April 2013, 88 samples tested positive from approximately 900 000 samples collected from different surveillance sites around the country. The samples were analysed by national and provincial avian influenza reference laboratories in China [19]. In December 2013, results from the national monitoring of influenza A(H7N9) conducted by the Chinese ministry of agriculture included 18 positive samples (virus genome) out of 200 tested (9.0%) from four sampling sites in Zhejiang; a further two (0.08%) samples (genomic) out of 2 521 tested positive from a total of 151 sampling sites in Guangdong [20,21]. In December 2014, 60 574 virological and 120 710 serological samples were collected from 7 379 sites in 24 provinces. Fourteen of these virological samples tested positive for A(H7N9); these samples came from Jiangsu (one chicken, one environmental sample), Zhejiang (six chickens, one duck), Fujian (one environmental sample) and Xinjiang Uygur autonomous region (two chickens, two environmental samples). Sites with positive samples included eight different live poultry markets and one backyard farm [22]. A number of peer-reviewed articles have summarised the results of surveillance activities since April

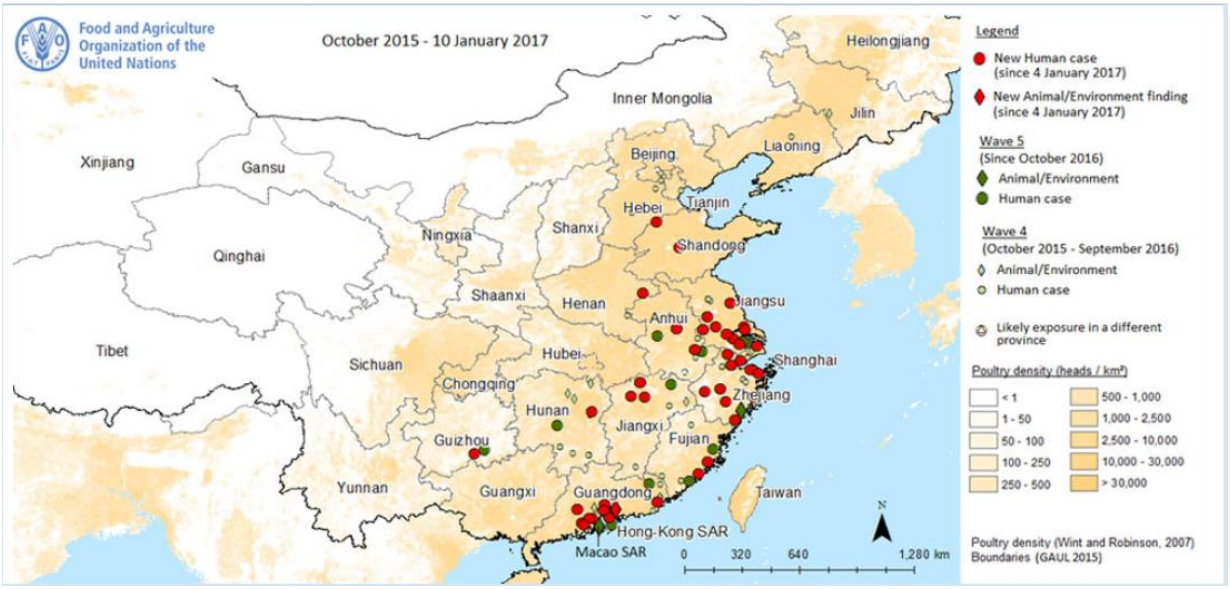
2013, citing a total of 71 920 samples, 1 728 (2.4%) of which tested positive for A(H7N9) (1 215 environmental samples, 501 chickens, one goose and one tree sparrow) [23].

The number of positive detections in poultry – and particularly the environment – seems to have considerably increased in the 2016–2017 epidemic wave, with 10–16% positivity in environmental samples. According to reports received by FAO on surveillance activities for A(H7N9) viruses in mainland China, positive samples continue to be detected mainly from live bird markets, vendors and some commercial or breeding farms. Several samples taken for the avian influenza monitoring programme in Anhui, Guangdong and Zhejiang in December 2016 tested positive for A(H7N9) [3].

A high number of positive specimens from environmental sources was reported from affected areas, e.g. in Huizhou, a city in southeast Guangdong [23]. In Jiangsu, 16% of environmental specimen collected from live poultry markets in December 2016 tested positive for H7. The Health and Family Planning Commission of Guangdong province reported that 60 (9.4%) out of 637 environmental samples collected from 21 live poultry markets in 15 cities in Guangdong in the first week of January 2017 tested positive for H7 virus. Of 181 139 serum and 53 102 virological samples collected in December 2016 at 7 605 locations in 28 provinces, eight virology samples tested positive for A(H7N9); these samples were taken from markets, a farm and a slaughterhouse in Zhejiang, Anhui, and Guangdong provinces. Of the collected serum samples, 349 tested positive for H7 antibodies from poultry farms (chickens, ducks and geese) or live bird markets in Gansu, Jiangsu, Qinghai, Shanxi, and Liaoning provinces [3,24]. In Macau, samples taken from a consignment of silky fowl in a wholesale poultry market tested positive for A(H7N9) on 13 December 2016.The affected silky fowl were imported from mainland China.

The map below (Figure 3) shows the geographic locations where human cases were reported, as well as locations of positive avian and environmental samples. For some cases, exposure may have occurred in a different geographic area.

Figure 3. Distribution of human cases of influenza A(H7N9) and positive avian and environmental samples, China, 1 October 2015 to 10 January 2017



Source: Food and Agriculture Organization of the United Nations (FAO), Emergency Prevention System for Transboundary Animal Diseases (EMPRES), Rome, Italy [23]

Applied control measures

The major source of infection with influenza A(H7N9) for humans is likely to be poultry or birds handled at live bird markets or backyard farms [25]. Wild birds act as reservoirs for the H7 and N9 genes of influenza viruses [26,27] while live bird markets seem to serve as amplifiers [28]. In 2013, the Chinese ministry of agriculture reported that 'stamping-out' control measures were being implemented in poultry markets, and that some markets were temporarily closed. These closures were associated with a decrease in the number of human cases of A(H7N9) in the relevant localities [28]. The closure of live poultry markets in the most affected cities helped to reduce the risk of A(H7N9) infection in humans.

In 2014, after the occurrence of human cases, the main cities in Guangdong and Zhejiang, but also in other provinces, closed live poultry markets, following the model applied in Shanghai and Hong Kong. In response to human cases in Guangdong in January 2015, the local authorities in Shenzhen city also closed all live bird markets [29].

In December and January 2017, according to FAO and the Chinese authorities, several cities in affected areas temporarily closed live bird markets, poultry wholesale markets, and farmers' poultry markets, or suspended all live

poultry trade either for the season or until further notice, e.g. in Guangdong (Guangzhou, Zhongshan, Zhaoqing); Jiangsu (Changzhou, Wuxi, Suzhou, and Jiangyin), Shanghai; Anhui (Bozhou, Wuhu); Zhejiang (Wencheng County, Yueqing, Rui'an and Lucheng districts of Wenzhou) [4,23,24]. In Zhejiang and Guangdong provinces, live poultry trade is currently prohibited and slaughter centralised [4,24].

A Chinese investigation team identified a higher contamination of the environment with A(H7N9) viruses and higher exposure levels as the reason and driver behind the upsurge in human cases since December 2016 [4].

Disease background

Clinical aspects, spectrum of disease and treatment

The median incubation period has been estimated to be six days (range: 1–10 days) [30]. Fever and cough have been the most common symptoms, while vomiting and diarrhoea have appeared in a smaller proportion of cases [7,31]. A high frequency of underlying medical comorbidities has also been reported [7,30]. Some milder cases were identified through extended testing of outpatients with influenza-like illness [32], suggesting that A(H7N9) presents with a broad clinical spectrum. In particular, paediatric A(H7N9) patients tend to present with clinically milder disease [33]. The symptomatic case-fatality risk was estimated between 160 (63–460) and 2 800 (1 000–9 400) per 100 000 symptomatic cases [34], suggesting that A(H7N9) infection is not as severe as A(H5N1) [35], but much more severe than A(H1N1)pdm09 [36]. The case fatality ratio has been relatively constant at around 40% over the years (Table 2). The presence of at least one chronic underlying condition has been demonstrated as a risk factor for A(H7N9) infection [25].

In China, contacts of cases are closely monitored to identify case clustering and potential human-to-human transmission. A few small family clusters were detected, showing high genomic sequence similarities and also reporting common exposure to risk sources (live bird market or dead poultry) prior to onset of symptoms [33,37,38]. While occasional human-to-human transmission in the clusters cannot be ruled out, sustained human-to-human transmission has not been observed [6,30]. Some studies identified seroconversion in up to 10% of asymptomatic close contacts of symptomatic A(H7N9) cases [39]. Serological studies in China found poultry workers as being seropositive for antibodies against A(H7N9) [40-42].

Studies of A(H7N9) viruses isolated from humans suggest that A(H7N9) is resistant to adamantane antiviral agents but susceptible to neuraminidase inhibitors oseltamivir and zanamivir [43-45]. However, reduced susceptibility to neuraminidase inhibitors has been documented in several cases after the start of oseltamivir treatment [46]. A few isolates also showed drug resistance to oseltamivir but sensitivity to peramivir [47]. WHO recommends antiviral treatment with a neuraminidase inhibitor as soon as possible for patients with suspected or confirmed A(H7N9) infection, but does not recommend routine post-exposure antiviral chemoprophylaxis for close contacts of confirmed influenza A(H7N9) cases. However, the initiation of empiric post-exposure antiviral treatment may be considered in certain circumstances, mainly in people with underlying medical conditions [48]. The US CDC has also published interim guidance on the use of antivirals for treatment of A(H7N9) infection [49] and for chemoprophylaxis of close contacts [50]. They recommend oseltamivir or inhaled zanamivir to close contacts of a confirmed or probable influenza A (H7N9) case depending on the risk of exposure. For high risk exposure (household or close family members), chemoprophylaxis should be administered while for moderate risk exposure (healthcare worker with higher risk-contact to case), chemoprophylaxis could be considered. The interim ECDC expert opinion suggests treatment of Influenza-like Illness (ILI) and laboratory confirmed influenza cases during zoonotic influenza outbreaks and considering prophylaxis for occupationally exposed persons [51].

Vaccines against avian influenza A(H7N9) infections in humans

The most important intervention in preparing for the pandemic potential of influenza A(H7N9) is the development and use of human vaccines, therefore the situation is being constantly monitored and assessed by WHO [52]. In May 2013, WHO published its first summary of development and release of candidate vaccine viruses for clinical trials [53]. Subsequently, nine candidate vaccine viruses have passed relevant safety testing and two-way haemagglutinin inhibition tests that allow them to be handled under BSL-2 enhanced containment [54]. After promising results of vaccine candidate testing in mice, chickens, ferrets and non-human primate models, several phase 1 clinical trials in healthy adults >18 years of age have been conducted. The vaccine candidates tested have, however, not been authorised for use.

Infection control measures in healthcare

WHO has produced a guidance document on laboratory biorisk management for A(H7N9) [55,56]. These guidelines are broadly applicable to the management of all human cases of avian influenza and related samples. WHO recommends that basic appropriate infection prevention and control measures (standard precautions) be consistently applied in all healthcare settings at all times, and that the health status of healthcare workers be

closely monitored. Together with standard precautions, healthcare workers caring for those suspected or confirmed to have A(H7N9) infection should use additional precautions.

Disease surveillance in Europe

Surveillance for respiratory infections in humans

All novel influenza strains are notifiable diseases in the EU. Notifications are carried out in accordance with Commission decisions and the International Health Regulations (IHR) through the Early Warning and Response System (EWRS) and IHR, respectively [57]. ECDC developed an interim case-finding algorithm and a case definition for disease surveillance and the reporting of patients infected by the avian influenza A(H7N9) virus in EU/EEA Member States [58]. Infectious disease protocols for case investigations are available from the Consortium for the Standardization of Influenza Seroepidemiology (CONSISE) [59] and national authorities. Agreed protocols for clinical investigations have been prepared by the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) [60].

Evidence of the effectiveness of contact tracing on board airlines in preventing the spread of infection is limited and should only be considered following a risk assessment on a case-by-case basis [61].

Diagnostics of avian influenza infections in humans

With routine diagnostic laboratory assays, the novel A(H7N9) 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, influenza A(H7N9) viruses are expected to be classified as un-subtypeable influenza A if no specific A(H7) diagnostic test is performed. It is standard procedure in diagnostic laboratories to send influenza A virus isolates or clinical samples that cannot be subtyped to the national reference laboratory (national influenza centres; NICs) and to a WHO Collaborating Centre for characterisation, as was done in China for the first influenza A(H7N9) isolates.

The European Reference Laboratory Network for Human Influenza (ERLI-Net) laboratories have rapidly developed and verified their capabilities for detecting the novel influenza A(H7N9) influenza virus [62]. In an external quality assessment RT-PCR detection panel which included an influenza A(H7N9) sample, 33 of the 36 participating EU/EEA laboratories from 29 countries detected the virus correctly as influenza A(H7) [63].

To assist European laboratories in verifying and ensuring their diagnostic capabilities with regard to avian influenza A(H7N9) virus, ECDC, ERLI-Net and the WHO Regional Office for Europe have released a technical briefing note on diagnostic preparedness in Europe for detection of avian influenza A(H7N9) viruses [64].

Discussion

Avian influenza A(H7N9) remains a widespread zoonotic disease in several provinces in China. The virus is transmitted sporadically to humans exposed to poultry, contaminated environment or live bird markets.

The notification of human cases of influenza A(H7N9) in China has followed a seasonal pattern, with peaks in winter months and sporadic cases in the summer. The second wave, in 2014, had a significantly larger amplitude than the first wave in 2013, both in terms of number of cases and geographic spread, suggesting that the virus became more widespread in its domestic bird reservoir, which, in turn, led to increased human exposure to the virus. The third and fourth waves had a lower magnitude, while the fifth epidemic seems to be following the pattern of the second wave with a high number of human cases. The age and sex distribution has remained comparable throughout the waves. There is no clear evidence of a trend towards increased severity of the disease in human cases. In addition, no viral markers for increased transmissibility to humans have been identified. WHO assesses the likelihood of sustained human-to-human transmission as low [65].

However, the more widespread distribution of cases, the high contamination of the environment and the increasing number of reported cases (also from rural sites), in conjunction with the large upsurge in cases since December 2016 mandates increased awareness and the implementation of strict infection prevention and control measures to reduce the number of severe human cases.

With the regular influenza season now ongoing in China and elsewhere in the northern hemisphere, there is a potential risk for co-infections with other influenza viruses and the occurrence of new reassortant viruses, with the possibility of increased capacity for transmission in the human population. As the seasonal influenza virus circulates in humans, there is an increased risk for reassortment of the seasonal influenza viruses with the avian influenza A(H7N9) viruses in co-infected humans, as well as an increased risk of reassortment with other circulating avian influenza viruses of the H5 type. In several patients, co-infections of A(H7N9) with seasonal influenza viruses have already been observed, either with A(H1N1)pdm09, A(H3N2) or B viruses [66-68]. Moreover, a nosocomial cluster of a co-infection of A(H7N9) and a seasonal A(H1N1)pdm09 influenza virus has been observed in two patients with severe underlying immunocompromised conditions [69]. Few clusters with human-to-human transmission have

been observed, and overall information to date suggests that these viruses do not transmit easily from human to human, and the investigations do not support sustained human-to-human transmission. Surveillance activities should be enhanced to also identify milder cases infected with avian influenza virus as the identification of cases tends to be more likely in severely ill persons [70].

The celebrations for the Chinese new year period might increase the potential for human exposure to both A(H7N9) and seasonal influenza viruses, thereby increasing the risk of reassortment in humans. During the holidays, demand for poultry usually increases, which also leads to an increase in poultry trade and additional exposure to the virus.

Domestic and international travel activities tend to spike during the first quarter of every year: according to a survey, 343 million Chinese are expected to travel during this period, with 82 percent of the respondents planning to travel in the first quarter of 2017, half of them during the Spring Festival holiday. According to the China National Tourism Administration, over six million Chinese tourists will travel abroad during the upcoming Spring Festival, mostly to neighbouring countries [71,72].

Between January and May 2015, of the 2 144 713 air travellers from the EU/EEA to China (Table 3), 21% were from the United Kingdom, 19% from Germany, and 15% from France. The number of travellers from and to Europe, however, decreases every year during the winter months (Figure 4, Table 3). Although no increase was observed in human cases due to A(H7N9) during and after previous Chinese New Year celebrations, travel-related cases have previously been identified outside of China, and the possibility of humans infected with A(H7N9) returning to the EU/EEA cannot be excluded.

Figure 4. Number of international travellers from EU/EEA countries to China and vice versa, per month, October 2011 to December 2015

Table 3. Air travel to and from China, reported and estimated number of passengers, by month, January to May 2015

Origin	Destination	Jan 2015	Feb 2015	Mar 2015	Apr 2015	May 2015
EU/EEA	China	352 497	378 211	459 412	469 104	485 489
China	EU/EEA	377 843	366 234	433 129	528 102	507 357

Source: International Air Transport Association (IATA)

Intervention strategies such as temporary closures of live poultry markets have shown an impact on the number of human infections [73,74]. Following the detection of A(H7N9) in poultry and environmental samples in 2016 and early 2017, many Chinese cities closed live bird markets to reduce the risk of human exposure. However, alternative and safer poultry processing may not be feasible in many parts of China, and poultry trade related to the Chinese New Year celebrations might continue in other places. It is unclear to what degree unauthorised and informal trade related to the upcoming festival activities will continue [16]. The disruption of established and formal trade patterns through local interventions such as live bird market closures might contribute to the spread of the virus through the movement of infected poultry to other provinces/locations. Harmonised strategies for the management of A(H7N9) in the poultry population and live bird markets across affected provinces might help to reduce the further geographical spread of the disease.

Awareness campaigns by the local and national Chinese public health authorities are ongoing in China to inform the population of the risk of infection associated with live poultry, wet markets, poultry farms or certain forms of contamination (e.g. bird droppings). Proper personal and hand hygiene as well as food hygiene recommendations have been communicated [3]. Chinese authorities have also strengthened surveillance for human cases. WHO advises that travellers should avoid visiting poultry farms, having contact with animals in live bird markets or slaughter areas and contact with surfaces potentially contaminated with droppings from poultry or other animals should be avoided. Proper hand hygiene and food safety are also recommended [1].

ECDC threat assessment for the EU

The A(H7N9) transmission pattern indicates a persistent zoonotic reservoir. The continued transmission of this reassortant avian influenza virus capable of causing severe disease in humans in one of the most densely populated areas in the world remains a cause for concern due to the potential for a pandemic virus to develop. However, the most likely current scenario for China is that these outbreaks remain local zoonotic outbreaks in which the virus is transmitted sporadically to humans in close contact with the animal reservoir, similar to the influenza A(H5N1) situation. A seasonal pattern in human infections, similar to seasonal influenza, appears to be emerging.

The epidemiology of the human cases has not changed during the most recent epidemics, however in the current wave more cases in rural areas have been detected, and cases are more widely distributed. This might be due to a change in the epidemiology of the disease in the reservoir (i.e. domestic poultry, with a higher circulation in poultry at the farm level than at live poultry markets). A higher virus circulation and prevalence in the poultry population would also contribute to increased contamination of the environment.

The recent upsurge of human cases due to a higher risk of exposure indicates the possibility of sporadic imported cases to Europe. Caution should be taken by people travelling to China to avoid direct exposure to poultry, live poultry markets or backyard farms. Travellers that have visited affected areas and develop respiratory symptoms and fever after their return should consult a physician and mention their recent travel history to initiate early diagnosis and treatment. The possibility of humans infected with A(H7N9) returning to the EU/EEA cannot be excluded. However, the risk of the disease spreading within Europe via humans is still considered low, as the virus does not transmit easily among people.

People in the EU presenting with severe respiratory or influenza-like infection and a history of travel to the affected areas in China with potential exposure to poultry or live bird markets will require careful investigation, management and infection control. Adequate samples for influenza tests should be rapidly taken and processed from patients with relevant exposure history within 10 days of symptom onset. Early or presumptive treatment with neuraminidase inhibitors should always be considered for suspect or confirmed cases, in line with relevant national and international recommendations. Contacts of confirmed cases should be followed-up, tested and offered post-exposure prophylaxis.

The risk of avian influenza viruses being transported to Europe in poultry through legal trade is negligible. EU regulations do not permit importation of live poultry, day-old chicks and hatching eggs and other birds (captive birds such as parrots, finches and ornamental birds) from China. The only poultry commodities authorised for import from China into the EU are sterilised meat products, heat-treated poultry meat from Shandong, and heat-treated egg products. Given the very heat-labile nature of all influenza viruses, these commodities are not considered to pose a risk of influenza virus transmission to consumers.

Considering the severity of the disease, the fact that limited human-to-human transmission cannot be excluded in some clusters, that no vaccine is available against A(H7N9), and the favourable safety profile of the antiviral drugs of choice, it is likely that the benefits of post-exposure chemoprophylaxis of close contacts with neuraminidase inhibitors outweigh the risks. Evidence of benefits and effectiveness of prophylaxis and treatment remain limited.

In order to decrease the risk of infection, EU citizens travelling or living in China should minimise their exposure to live poultry markets, avoid contact with live or dead poultry or their products, and practice good hand hygiene when visiting places with birds or poultry [75].

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