



RAPID RISK ASSESSMENT

Human infection with avian influenza A(H5N1) virus, Egypt

23 December 2014

Main conclusions and recommendations

- Influenza A(H5N1) has been circulating in domestic poultry in Egypt since its introduction in 2006 and has been the source of sporadic human infections.
- The number of cases reported in Egypt is higher than compared to last year, although in the same range as in 2012, but the number of laboratory-confirmed human cases of avian influenza A(H5N1) virus infection reported in November by Egypt is the highest ever reported for that month.
- The locations of the reported cases of A(H5N1) in humans match the locations of outbreaks in backyard poultry and, in addition, the reported human cases had direct exposure to infected poultry.
- As the affected regions are non-touristic areas, the risk for EU citizens is considered extremely low.
- The increase in the number of human cases reported in Egypt in 2014 does not change the current risk status of this epidemic.

Source and date of request

ECDC Internal Decision, 10 December 2014

Public health issue

This document aims to:

- summarise the epidemiological, virological and environmental information about human infections with avian influenza A viruses of subtype A(H5N1) in Egypt;
- assess potential changes in the risk to public health in the EU/EEA and to EU/EEA citizens.

Consulted experts

ECDC internal response team (in alphabetical order): Kaja Kaasik Aaslav, Cornelia Adlhoch, Tarik Derrough, Emmanuel Robesyn, Pasi Penttinen

External contributors (in alphabetical order): Ana Paula Coutinho (WHO Regional Office for Europe), Manal Fahim, Samir Refaey, Ahmed Zaghoul (all Epidemiology and Surveillance Unit, Ministry of Health and Population, Egypt), Soheir Hassan Abd El Kader (General Organisation for Veterinary Services, Ministry of Agriculture, Egypt)

Disease background information

Highly pathogenic avian influenza (HPAI) virus type A(H5N1) is highly infectious for a number of bird species, including most species of domestic poultry [1-4]. Unlike most other avian influenza viruses, this virus type is also highly pathogenic for humans. However, the viruses remain poorly adapted to humans, and transmission from birds to humans is infrequent [5-9]. Since the first human epidemics of A(H5N1), limited clusters of human cases have been reported but no sustained human-to-human transmission has been observed. Zoonotic transmission to humans from infected birds occurs either directly or through environmental contamination. Hence, almost all human infections have been related to close contact with infected or sick birds or their faecal products in domestic settings, e.g. in 'wet markets' in Asia [8].

The most commonly identified risk factors associated with A(H5N1) virus infection include contact with infected blood or bodily fluids of infected poultry via food preparation practices; touching and caring for infected poultry; exposure to H5N1 via swimming or bathing in potentially virus-laden ponds; and exposure to H5N1 at live bird markets [10]. WHO has published a proposal for candidate vaccine viruses for pandemic preparedness [11].

Since 1996, when they were first observed in China, A(H5N1) viruses have affected poultry, initially in the Far East and later in parts of Europe, the Middle East and Africa [12]. The virus was introduced into Egypt in 2006, and since then a separate virus clade has evolved from the strains in Asia [13].

The first human case of A(H5N1) avian influenza in Egypt was diagnosed in 2006 [14]. Raising poultry in households is common in Egypt, where community awareness of the risks of avian influenza is low. Since the initial response in 2006, which attempted to eradicate disease outbreaks in poultry, Egyptian veterinary authorities have faced difficulties in controlling the disease due to the high density of commercial and household poultry flocks, the intensity of bird movements, and breaches in bio-security. Inadequate compensation for culled birds, inappropriate use of vaccine, and the exclusion of household poultry from vaccination programmes have further contributed to the reduced efficiency of veterinary control. The capacity of veterinary services in investigating outbreaks and carrying out surveillance are challenged by limited resources e.g. manpower, vehicles and equipment.

The public health impact of the vaccination programme in poultry against HPAI has been limited, as it does not prevent shedding and human exposure to the virus, although it reduces the severity of clinical signs and mortality of vaccinated poultry.

Human and avian surveillance of A(H5N1) in Egypt

Influenza is a notifiable disease in Egypt, and the country has well-established sentinel surveillance systems for influenza-like illnesses (ILI) and acute respiratory infections (ARI), covering 15 public (ministry of health) hospitals and one polyclinic. Since 2006, all healthcare facilities have been obliged to notify suspected A(H5N1) cases – ILI/ARI with bird contact – and confirmed, PCR-positive cases to the Ministry of Health. A hospital-based surveillance system was established in 2009 to report ILI/severe acute respiratory infection (SARI)/pneumonia cases, and samples from severe SARI/pneumonia cases or cases without clear diagnosis are sent to laboratory to be tested for influenza viruses and MERS-CoV.

A recent study estimated that the seroprevalence of anti-A(H5N1) antibodies (titre \geq 80) among Egyptians who are exposed to poultry was 2% [15].

Egypt has implemented a routine nationwide avian influenza surveillance programme after a ministerial decree (number 221) in 2006. The National Laboratory for Veterinary Quality Control on Poultry Production is in charge of the official diagnosis and surveillance of avian influenza virus in Egypt. Between 2009 and 2010, tracheal and cloacal swabs were collected from domestic poultry from 22 024 commercial farms, 1 435 backyards and 944 live bird markets, as well as from 1 297 wild birds representing 28 different types of migratory birds [16].

Human and avian surveillance of A(H5N1) in Europe

All novel influenza strains are notifiable diseases in the EU under EU legislation and the International Health Regulations (IHR) through the Early Warning and Response System (EWRS) and IHR, respectively. Human infections with A(H5N1) are notifiable according to EU Decision 1082/2013/EU [17,18].

EU legislation for surveillance and control of highly pathogenic avian influenza viruses in bird species is in place [19,20].

Event background information

Human cases in the world

From 2003 to 4 December 2014, 676 laboratory-confirmed human cases of avian influenza A(H5N1) virus infection, including 398 deaths, have been reported to WHO from 16 countries (Table 1, Figure 1) [14].

The total number of human cases due to A(H5N1) is decreasing; 2014 had the lowest number of cases reported since the first cases in 2003 (Table 1). The most affected countries cumulatively are Indonesia and Egypt. In 2014, Egypt and Cambodia reported the most cases (Table 1).

Whenever avian influenza viruses are circulating in poultry, sporadic infections or small clusters of human cases are possible in people exposed to infected poultry or contaminated environments, especially in households. Human infections remain rare, and influenza A(H5N1) viruses do not currently appear to transmit easily among people. As such, the risk of community-level spread of these viruses remains low [14].

Table 1. Distribution of A(H5N1) cases by country and year, February 2003 to 4 December 2014

Reporting country	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
Azerbaijan				8									8
Bangladesh						1			2	3	1		7
Cambodia			4	2	1	1	1	1	8	3	26	9	56
Canada											1		1
China	1		8	13	5	4	7	2	1	2	2	2	47
Djibouti				1									1
Egypt				18	25	8	39	29	39	11	4	12	185
Indonesia			20	55	42	24	21	9	12	9	3	2	197
Iraq				3									3
Laos					2								2
Myanmar					1								1
Nigeria					1								1
Pakistan					3								3
Thailand		17	5	3									25
Turkey				12									12
Vietnam	3	29	61		8	6	5	7		4	2	2	127
Total	4	46	98	115	88	44	73	48	62	32	39	27	676

Human cases in Egypt

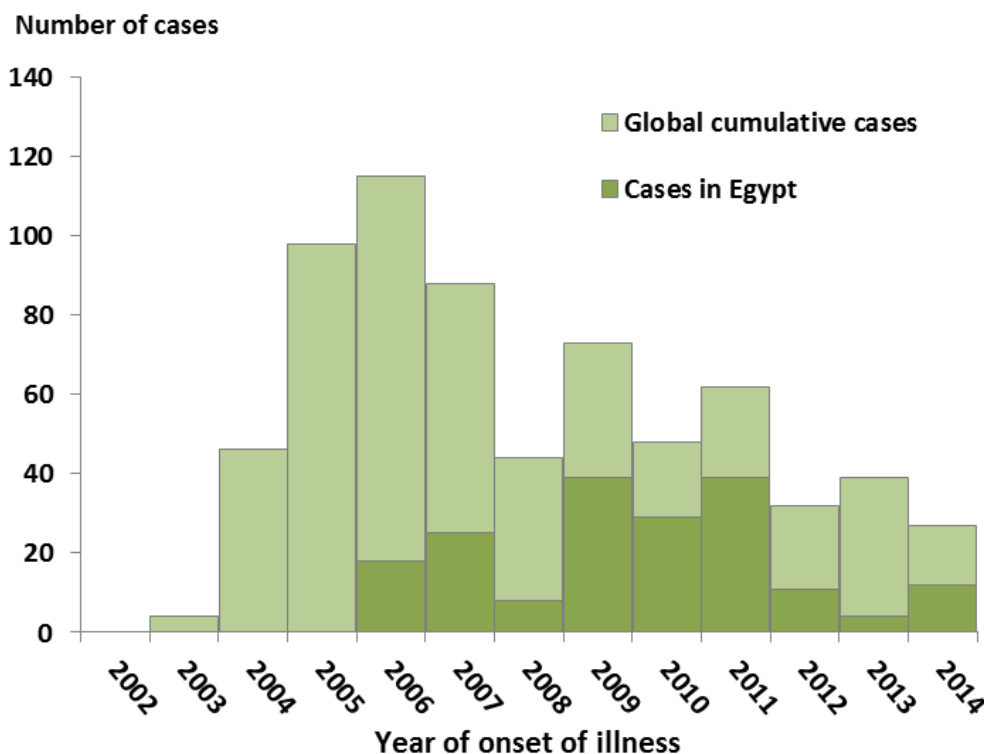
According to a WHO update published on 4 December 2014, and since the last WHO update dated 2 October 2014, eight new human cases of influenza A(H5N1) have been reported in Egypt, with onset of disease in November 2014, bringing the total for 2014 to 12. Additionally, the Egyptian authorities reported an overall number of 20 confirmed cases for 2014, not all WHO confirmed yet. This is a higher number than in 2013, although in the same range as in 2012. This is also the highest number of laboratory-confirmed human cases of avian influenza A(H5N1) virus reported by Egypt in the month of November (Figure 2). The number of fatal cases in 2014 is within the same range as in the previous two years (Table 2). The number of human cases of A(H5N1) has varied each year since its introduction in 2006 (Figure 1).

Table 2. H5N1, number of cases and deaths in Egypt, 2006–2014 (as of 4 December 2014)

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014
Number of cases	18	25	8	39	29	39	11	4	12
Number of deaths	10	9	4	4	13	15	5	3	5

Source: WHO [14]

Figure 1. Cumulative number of global confirmed human cases of avian influenza A(H5N1) reported to WHO, 2003–2014, as of 4 December 2014

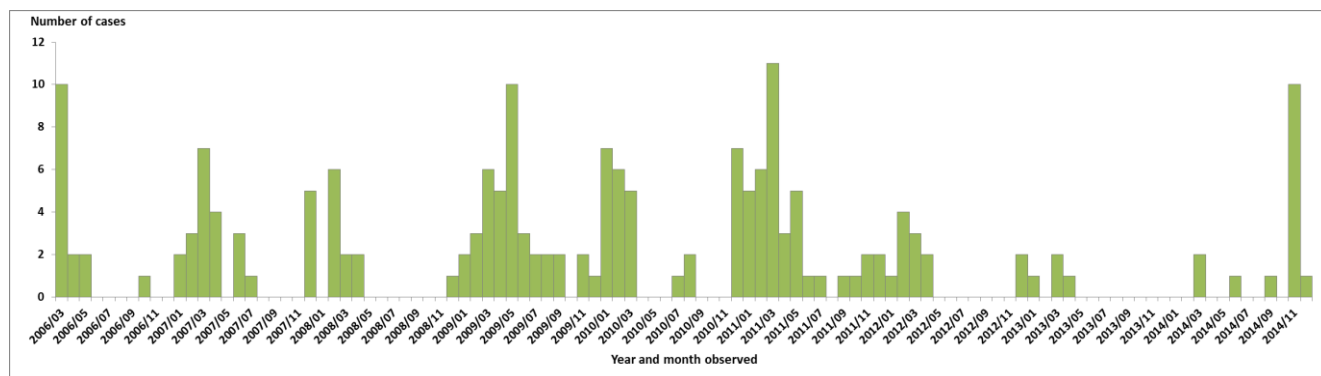


As of 22 December 2014, a total of 20 confirmed cases due to A(H5N1), including nine fatalities, have been reported for 2014 by the Egyptian Ministry of Health. A median age of 22 years was observed, ranging from 1.4 to 56 years. Fourteen cases were female and fourteen reside in rural areas. Most cases reported contact with apparently healthy, sick, or dead backyard poultry.

No clustering of cases has been observed in any of the affected districts and villages. The location of the human cases overlaps with areas of reported outbreaks of A(H5N1) in domestic poultry. Most cases are reported from central Egypt along the Nile river and in the Nile delta (Figure 3).

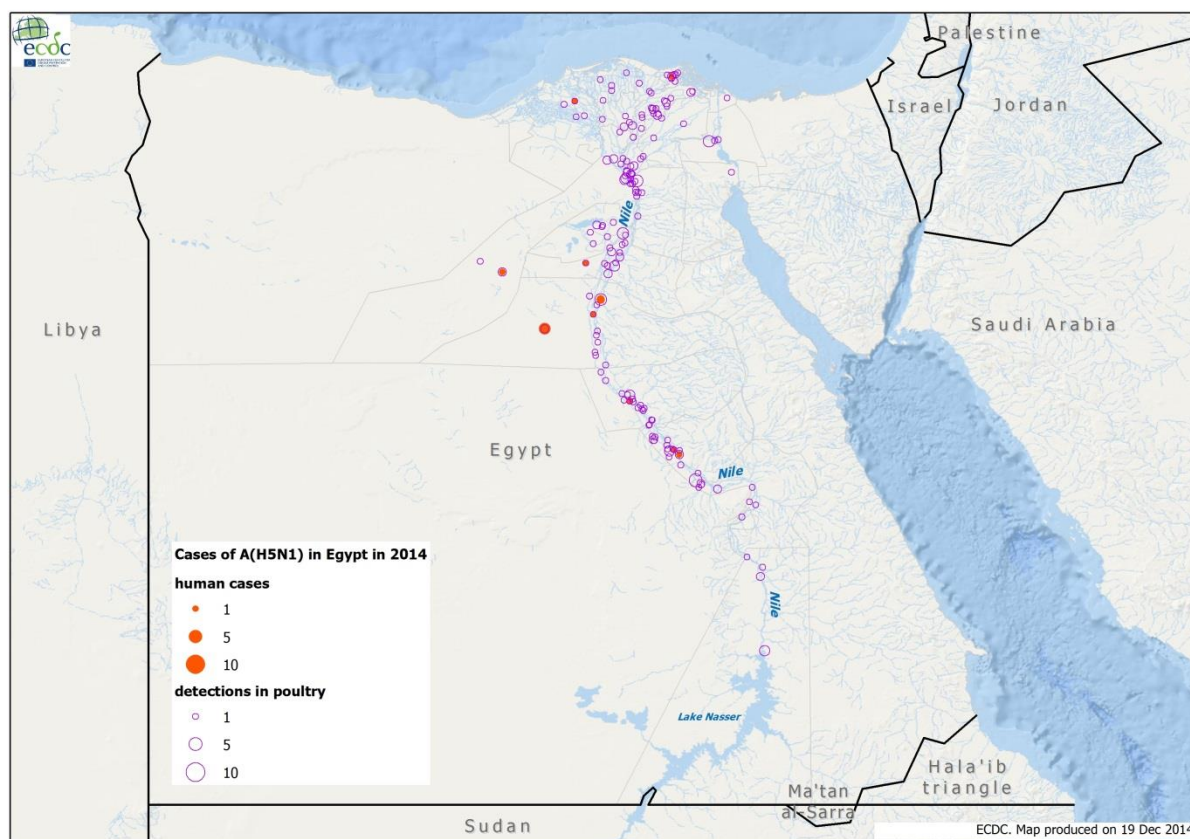
Preliminary laboratory investigations did not detect any changes in the viruses isolated from the patients compared to isolates from previously reported cases. The occurrence of two mutations in A(H5N1) isolates from poultry have been recorded in Egypt. According to the Reference Laboratory for Veterinary Quality Control on Poultry Production, these mutations were first detected in 2011 and are located at sites (α129 and α151). Further investigations into the significance of these mutations are needed.

Figure 2. Number of human cases of A(H5N1) observed in Egypt, by year and month, March 2006 to December 2014



Source: EMPRES-i; available from: <http://empres-i.fao.org/eipws3q>; accessed 19 Dec 2014

Figure 3. Geographic distribution of human cases and outbreaks of A(H5N1) in poultry reported in 2014, Egypt



Source: EMPRES-i; available from: <http://empres-i.fao.org/eipws3g>; accessed 19 Dec 2014

ECDC threat assessment for the EU

- Human infections remain rare, and influenza A(H5N1) viruses do not currently appear to transmit easily among people. As such, the risk of community-level spread of these viruses remains low, and the assessment of the last updated ECDC Rapid Risk Assessment published on 26 February 2014 remains valid [21].
- A higher number of human cases due to A(H5N1) was reported from Egypt in November 2014. The detection of A(H5N1) in backyard poultry with a high number of outbreaks in 2014 might be the cause for the increase in human cases, as all cases reported exposure to infected poultry prior to the onset of symptoms.
- No indication is given of human clusters or human-to-human transmission.
- Considering the circulation of the virus in non-touristic areas, the risk of EU citizens being infected is extremely low. No cases of A(H5N1) among travellers to Egypt have ever been notified.

Conclusions

The recently reported increase of human cases of A(H5N1) infection from Egypt in November 2014 might be due to an increase in the circulation of A(H5N1) in backyard poultry and exposure to infected poultry across Egypt. Identification of such sporadic cases or small clusters are not unexpected as avian influenza A(H5N1) viruses are known to be circulating in poultry in the country. Strict control measures of infected poultry are essential to prevent zoonotic transmission and human cases. Epidemiological investigations should be performed and results communicated to the global public health community.

Human cases and outbreaks were only reported from non-touristic areas in Egypt. Travellers visiting affected areas should avoid contact to sick or dead poultry and birds.

References

1. Influenza team European Centre of Disease P, Control. Avian influenza update: recent outbreaks of H5N1 in poultry worldwide. *Euro Surveill.* 2007 Jan;12(1):E070125 2.
2. Swayne DE, Pantin-Jackwood M. Pathogenicity of avian influenza viruses in poultry. *Dev Biol (Basel).* 2006;124:61-7.
3. Brown IH, Banks J, Manvell RJ, Essen SC, Shell W, Slomka M, et al. Recent epidemiology and ecology of influenza A viruses in avian species in Europe and the Middle East. *Dev Biol (Basel).* 2006;124:45-50.
4. Kelly TR, Hawkins MG, Sandrock CE, Boyce WM. A review of highly pathogenic avian influenza in birds, with an emphasis on Asian H5N1 and recommendations for prevention and control. *J Avian Med Surg.* 2008 Mar;22(1):1-16.
5. Thanh TT, van Doorn HR, de Jong MD. Human H5N1 influenza: current insight into pathogenesis. *Int J Biochem Cell Biol.* 2008;40(12):2671-4.
6. Malik Peiris JS. Avian influenza viruses in humans. *Rev Sci Tech.* 2009 Apr;28(1):161-73.
7. Korteweg C, Gu J. Pathology, molecular biology, and pathogenesis of avian influenza A(H5N1) infection in humans. *Am J Pathol.* 2008 May;172(5):1155-70.
8. Nicoll A. (Yet) another human A/H5N1 influenza case and cluster – when should Europe be concerned? *Euro Surveill.* 2008 Apr 10;13(15).
9. De Martin S, Nicoll A, Coulombier D. A/H5N1 in the European Union: current levels of risk to humans, and responding to human cases and outbreaks. *Euro Surveill.* 2006;11(11):203-4.
10. Van Kerkhove MD, Mumford E, Mounts AW, Bresee J, Ly S, Bridges CB, et al. Highly pathogenic avian influenza (H5N1): pathways of exposure at the animal-human interface, a systematic review. *PLoS One.* 2011;6(1):e14582.
11. World Health Organization (WHO). Antigenic and genetic characteristics of zoonotic influenza viruses and development of candidate vaccine viruses for pandemic preparedness [17 Nov 2014]. Available from: http://www.who.int/influenza/vaccines/virus/201409_zoonotic_vaccinevirusupdate.pdf.
12. World Organisation for Animal Health (OIE). Facts & Figures: H5N1 Timeline [4 Dec 2014]. Available from: http://web.oie.int/eng/info_ev/en_AI_factoids_H5N1_Timeline.htm.
13. World Organisation for Animal Health (OIE). Update on highly pathogenic avian influenza in animals (type H5 and H7) 2014 [15 Dec 2014]. Available from: <http://www.oie.int/animal-health-in-the-world/update-on-avian-influenza/2014/>.
14. World Health Organization (WHO). Monthly Risk Assessment Summary as of 4 December 2014 2014 [15 Dec 2014]. Available from: http://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_04December2014.pdf.
15. Gomaa MR, Kayed AS, Elabd MA, Zeid DA, Zaki SA, El Rifay AS, et al. Avian Influenza A(H5N1) and A(H9N2) Seroprevalence and Risk Factors for Infection Among Egyptians: A Prospective, Controlled Seroepidemiological Study. *J Infect Dis.* 2014 Oct 29.
16. El-Zoghby EF, Aly MM, Nasef SA, Hassan MK, Arafa AS, Selim AA, et al. Surveillance on A/H5N1 virus in domestic poultry and wild birds in Egypt. *Virol J.* 2013;10:203.
17. European Parliament and of the Council. Commission Implementing Decision of 8 August 2012 [20 Feb 2014]. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:262:0001:0057:EN:PDF>.
18. European Parliament and of the Council. Decision 1082/2013/EU 2013. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:293:0001:0015:EN:PDF>.
19. World Organisation for Animal Health (OIE). Terrestrial Animal Health Code (2014) [19 Nov 2014]. Available from: <http://www.oie.int/international-standard-setting/terrestrial-code/access-online/>.
20. European Commission. Council Directive 2005/94/EC of 20 December 2005 on Community measures for the control of avian influenza and repealing Directive 92/40/EEC [10 Nov 2014]. Available from: <http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1415609228714&uri=CELEX:32005L0094>.
21. European Centre for Disease Prevention and Control (ECDC). Human infection with avian influenza A viruses, China - 24 Feb 2014 Stockholm: ECDC; 2014. Available from: <http://ecdc.europa.eu/en/publications/Publications/avian-flu-china-rapid-risk-assessment-26022014.pdf>.