RAPID RISK ASSESSMENT

A(H5N1) Highly Pathogenic Avian Influenza in Egypt – Implications for human health in Europe

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Conclusions and recommendations

Highly pathogenic avian influenza A(H5N1) infections are continuing to occur in poultry and humans in Egypt. However there is no evidence of a significant change in the pattern of human illness and deaths related to A(H5N1) virus infections in the country. Certainly there are no epidemiological data or analyses consistent with adaptation of these viruses to humans. Although the limited virological analyses carried out may indicate that the risk of an A(H5N1) pandemic emerging could be greater in Egypt than other countries, the implications of these analyses are difficult to interpret.

The first human cases in Egypt occurred in 2006. However, the risk of pandemic A(H5N1) viruses emerging in Egypt cannot be excluded and the continuing transmission of the virus among domestic poultry and on to humans in Egypt over the past five years is worrying. Egypt's proximity to EU/EEA countries increases the concern since a pandemic strain, if it emerged, would presumably spread to Europe very quickly. Despite the lack of evidence that the risk might be increasing, intensification of veterinary control measures in Egypt is due to concerns over human health.

Constant vigilance should be maintained for any enlargement in human A(H5N1) cluster size, other changes in the behaviour of the virus and/or individual human cases outside of countries like Egypt where the virus is recognised as being entrenched in domestic poultry.

Public health issue

Continuing occurrence of infections with highly pathogenic avian influenza A(H5N1) viruses in humans and poultry in Egypt and concern that the veterinary control measures may be insufficient to keep a check on continuing outbreaks in poultry, with potential implications for human health in Europe.

Event background information

Following a report to the media from the United Nations Food and Agriculture Organization (FAO) suggesting that the risks of A(H5N1) infection were changing, ECDC decided to undertake a rapid risk assessment in late August concerning the risks of A(H5N1) globally. The assessment concluded that there was no evidence of any increased risk to human health in Europe (1). This view was supported by the World Health Organization (WHO) and the World Organization for Animal Health (OIE) (2–3). The European Commission then asked ECDC whether it considered that the risk to humans had specifically changed for Europe as a result of the epidemiological situation in Egypt, which is the closest country with ongoing transmission of A(H5N1) viruses among poultry.

Consulted experts

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Disease background information

Influenza viruses type A(H5N1) are a group of avian viruses that are highly infectious for a number of bird species, including most species of domestic poultry (4–10). Unlike other avian influenza viruses, this virus type is also highly pathogenic for humans. The average case fatality rate (CFR) among reported cases remains substantial – over 50% in 2011 (6).

However, the viruses remain poorly adapted to humans and transmission from birds to humans is infrequent (5,9,10). Transmission to humans from birds is either direct 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 (2, 4–12). Human-to-human transmission has occurred since the first reports of the A(H5N1) viruses, but it is even less common than bird-to-human transmission and the effective reproductive number 'R' for human-to-human spread remains well under one (4,7,9,10).

Since 1996, when they were first observed in China, the A(H5N1) viruses have affected poultry, initially in the Far East and later in parts of Europe, the Middle East and Africa (2). The infection is currently considered entrenched in poultry, at least in parts of Bangladesh, China, Cambodia, Egypt, India, Indonesia and Viet Nam. In Egypt, human cases have been reported annually since 2006 (2,6). However, the viruses have also been reported intermittently in poultry and wild birds in other countries, including Europe (2,11–13).

The first human case of A(H5N1) avian influenza in Egypt was diagnosed in 2006 (2). Since their initial response in 2006, which attempted to eradicate disease outbreaks in poultry, Egyptian veterinary authorities have faced difficulties in controlling the disease due to a high density of commercial and household poultry flocks, the intensity of bird movements and breaches in bio-security. Inadequate compensation for birds culled, 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 the high number of outbreaks (14). The recent political instability in Egypt is an additional element that may lead to further difficulties in implementing an effective disease control policy.

Between 2005 and 2008, there were a number of reports of cases in wild and some domestic birds in EU/EEA countries. This led to greater awareness, more testing and increased bio-security in industrial settings (2). However, in the WHO European Region, the last recorded events date from 2010, when a large number of infected wild birds were found dead in the Tyva Republic of the Russian Federation (15), two backyard poultry outbreaks occurred in Romania (13,16), and a buzzard was found to be infected in Bulgaria (17). To date in 2011, there have been no reports of A(H5N1) infections in avian species or humans in the European Region but the risk of virus incursions to European poultry remains. Egypt's geographical proximity to Europe could make a virus incursion from Egypt to the European Union possible. The risk to neighbouring countries has been shown by an outbreak in Israel in March this year, where the virus detected came from the group of contemporary Egyptian viruses (13).

Since 2003, a total of 565 human cases of avian influenza A(H5N1) have been reported to the World Health Organization (WHO) (as at 19 August 2011). These reports originate from 15 countries and include 331 deaths, resulting in a case fatality rate (CFR) of 59% (6). The majority of cases occurred in people who had been in contact with domestic poultry or contaminated environments. Moreover, there are often reports of associated local die-offs of poultry (2). The CFR is very high compared to that for other animal or human influenzas infecting humans (5).

It is recognised that the human cases are underestimated, but assessing the correct numbers is complicated by the poor immunological response to these viruses in humans, who may be infected but only show a transitory immunological reaction (20). In addition, weaknesses in human health and laboratory services in the affected countries mean that human cases will go undetected. However, early care-seeking will increase the number of reported mild human cases if respiratory specimens are collected and transported promptly, and reliable laboratory testing is performed.

In 2011, WHO has reported 49 cases and 25 deaths from four countries: Bangladesh (two cases – no deaths), Cambodia (eight cases – eight deaths), Egypt (32 cases – 12 deaths) and Indonesia (seven cases – five deaths) (as at 19 August 2011) (6). The true level of infection and distribution of A(H5N1) among poultry and wild birds is

difficult to know because of inherent weaknesses in surveillance and laboratory capacity in many countries, especially those with limited resources. The same is true for surveillance of human cases (18).

A(H5N1) viruses remain a concern for human health in Europe due to four unusual characteristics:

- They often result in severe disease in humans, more so than for any other animal influenza;
- They are a persistent zoonotic infection among types of birds which humans are in close contact with in many countries;
- They are evolving continuously;
- They represent a threat because of the risk of mutation or genetic recombination with influenza viruses better adapted to and transmissible among humans (2,6).

Hence, persistent outbreaks in domestic poultry or wild bird populations, changes in distribution of the outbreaks or developments in the viruses are of importance and need to be carefully monitored, even if infections are mostly confined to birds.

ECDC risk assessment for the EU/EEA countries

The epidemiology of human infections in Egypt has always been different from other countries where A(H5N1) is entrenched in poultry. There are seasonal trends in some countries, with infections being more common in the colder months. However, what is particularly significant in Egypt is that the case fatality rate (CFR) in reported cases is lower than in other countries: 34% in Egypt versus nearly 60% at worldwide level (6).

At least two hypotheses exist to explain these observations with different implications:

- There is one published paper (Watanabe et al) reporting the ability of clades of A(H5N1) viruses isolated in Egypt to bind to human host cells, especially from the upper respiratory tract. The ability was higher than that for viruses from Asia (19). Hence, some authorities suggest this is an ominous sign of adaptation to humans.
- The other hypothesis, suggested by the majority of observers, is that the lower CFR in Egypt is a consequence of a combination of two factors. These are children being infected by a lower dose of virus acquired from the environment (than say adults who may be exposed to high doses while slaughtering poultry), plus greater awareness of human A(H5N1). This implies increased care-seeking by parents for their children, good access to health care and rapid diagnosis of suspected cases. It is suggested that these aspects are more lacking in other countries.

Those supporting the second hypothesis point out that the low CFR has not been linked to any progressive adaptation of the virus to humans. From 2006 to 2011, there was no trend in the annual CFR in human cases in Egypt. Watanabe et al suggest that their findings of a change in the virus binding may account for more reported human infections in Egypt and a lower CFR than in Asian countries such as Cambodia where all eight cases reported this year have had a lethal outcome. However, at the same time they note no indication of increased human-to-human transmission (19).

The second hypothesis is more plausible, and supported by observers who have been to the country. However, the uncertainty raises the difficulty of undertaking virological risk assessments for animal influenza and attempting to judge whether particular viruses have a greater pandemic potential. There are efforts to approach this issue, with a meeting convened by the United States CDC in October 2011 and an initiative underway from the European Food Safety Authority (EFSA).

Conclusions

There is no evidence of an important change in the human morbidity and mortality trends in relation to A(H5N1) in Egypt. Available data and information do not indicate a major change in the human epidemiology of A(H5N1) or, more specifically, in the adaptation of the virus to humans. There are only limited virological data suggesting that an A(H5N1) pandemic could emerge from Egypt. However, that risk cannot be excluded and it is worrying to see that transmission of the virus among domestic poultry and on to humans has been going on for five years so close to EU/EEA countries, since a pandemic strain could presumably spread to Europe very rapidly. Despite the lack of evidence that the risk might be increasing, intensification of veterinary control measures in Egypt is due to concerns over human health.

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