

Background Paper

2.1. b Trends and dynamics of HPAI – epidemiological and animal health risks

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Summary

The H5N1 HPAI situation has improved during the past 3 years with many countries managing to eradicate or control the disease. The tools and methods defined by the specialized technical agencies, FAO and OIE, work if they are implemented appropriately. Around 15 countries have been infected or re-infected during the past 8 months but the early detection and response have allowed most of them to eliminate outbreaks rapidly. Although the awareness and preparedness has improved considerably, the risk of re-incursion remains since H5N1 HPAI viruses are well entrenched in several countries through Asia and Africa with the situation in Indonesia, Egypt and Nigeria a serious concern. The risk of emergence of a new human pandemic virus remains as long as multiplication of these viruses is poorly controlled in poultry.

H5N1 HPAI viruses continue to evolve through both reassortment and point mutations resulting in the emergence of new genotypes, considerable variation within existing HA subclades and also emergence of at least one new clade that differed antigenically from existing viruses.

The source of most cases of HPAI is not determined. Epidemiological studies are hampered by limited surveillance data and investigations. Even when these are performed it is not always possible to determine the precise origin of infection.

Based on recent experiences likely risk factors for incursion of virus into a country or flock are becoming clearer. It is also possible to predict the likely outcome after incursion, particularly whether infection is expected to become entrenched.

Gains will continue to be made locally in controlling and preventing H5N1 HPAI but global eradication of H5N1 HPAI viruses remains a distant and unlikely prospect particularly if high risk production and marketing practices persist. Improvement of epidemio-surveillance and early response capabilities remain indispensable, including the strengthening of veterinary services and the development of strong public-private partnerships.

Highly pathogenic viruses of the H5N1 subtype have been causing disease in Asia since 1996. In 2003-04, infection was reported in a number of Asian countries and in 2005-06 there was spread of this virus to Central Asia, the Middle East, Europe and Africa. This paper reviews the current state of knowledge regarding the epidemiological features of this disease and the viruses that cause it.

Considerable improvements have been achieved in preventing and controlling HPAI in poultry during the past few years, which demonstrates that the tools and methods described in the FAO-OIE Global Strategy work when implemented appropriately.

Several countries in Asia that were previously heavily infected have managed to contain the disease and to reduce the quantities of circulating virus (Thailand, Viet Nam, and China). Early detection and response have succeeded in eliminating the outbreaks in countries that have been infected or re-infected during the past 8 months (Republic of Korea, Malaysia, Japan, Kuwait, Saudi Arabia, United Kingdom, Hungary, Turkey). This showed that a high degree of awareness and preparedness has been reached in these countries. Other countries have also shown improvement in their capabilities to detect and respond to new outbreaks, including Cambodia, Lao PDR, Pakistan and Myanmar.

The negative aspect is that H5N1 HPAI remains well entrenched in a number of countries in Asia and Africa. This puts neighboring or distant countries at permanent risk of incursion as demonstrated by the abovementioned new cases of H5N1 HPAI in poultry in late 2006 and the first half of 2007 and those in other recently infected countries such as Bangladesh and Ghana, which represent significant concerns.

In places where these viruses remain entrenched or multiply freely in poultry the risk of emergence of a human pandemic virus still exists.

In very few of these outbreaks has the route of entry of virus onto the index farm(s) been determined. There is a high level of suspicion of wild bird origin for recent (2006-07) Korean and Japanese outbreaks; genetic information available so far indicates a common source for both countries and the viruses belong to sub-clade 2.2, which is closely associated with wild birds. Trade in poultry or other birds is considered the most likely source of introduction for Kuwait, Saudi Arabia, and Ghana. The potential role of imported falcons warrants further exploration in the Middle East.

Detailed epidemiological investigations of the 2007 outbreak in turkeys in Suffolk, England highlight the difficulties faced in determining the exact source of virus through tracing, and the value of genetic studies of viruses in providing clues to possible origin. The virus isolated from turkeys in England was almost identical to other viruses detected at about the same time from commercial geese in Hungary (DEFRA 2007). This outbreak appeared to arise following the unlikely occurrence of a series of low probability events, facilitated by the close location of a poultry processing plant and the production areas. This outbreak also provided reminders that early cases of infection in a flock can be silent.

In places with entrenched infection, factors associated with poultry production and trade are implicated as the main routes of introduction to previously uninfected flocks. In Viet Nam, H5N1 HPAI viruses have continued circulating sub-clinically in unvaccinated domestic ducks. An increase in the prevalence of disease in May-June 2007 coincided with considerable seasonal expansion of the population of unvaccinated juvenile domestic ducks reared to graze harvested paddy fields.

Molecular studies indicate that new virus incursions occurred into countries in south east Asian countries in 2006 (subclade 2.3) but the mode of introduction was not determined. In Malaysia fighting cocks have been implicated as a source of infection.

Viruses in neighbouring areas appear to be genetically similar (e.g. Guangxi and Vietnam; Yunnan and Myanmar) (WHO 2007, Smith et al 2006a).

Experiences from the past years allow some assessment of the factors that appear to increase the risk of incursion of virus into uninfected countries or parts of countries. These include infection in a neighbouring country, movement of Anatidae (ducks, geese and swans) from infected places and the level of trade in poultry, poultry products and other birds from infected places, with a much higher weighting given to illegal or unregulated trade than trade conducted in accordance with international and regional standards (with the case in England providing a reminder that compliance with these standards markedly reduces but does not totally eliminate risk). The precise weighting of these risk factors varies from country to country.

The probability of disease occurrence in any particular flock is determined by a complex interplay between the level of threat of infection and the preventive measures used. Many high risk production and marketing practices remain across all FAO poultry production systems, especially but, not only, in systems 2 to 4¹. Unless these practices are modified in some way, or other risk mitigation measures are implemented then recurrent infection is likely in such farms and markets in those places where the threat of exposure to virus persists.

For example, in Indonesia, the system of marketing involves a large number of live poultry markets (>13,000) and many 'collectors' yards where birds from different origins are mixed. Preliminary studies² suggest that a high proportion of collector's yards are infected and this correlates with experiences in other countries in which poorly regulated live poultry markets have been shown to be infected. Until such time as the marketing system for broiler chickens in Indonesia is modified to minimise the likelihood of entry and persistence of H5N1 HPAI viruses there is little chance of sustained success in controlling this disease.

Levels of infection and disease associated with H5N1 HPAI viruses have been shown to vary over time. Seasonal peaks, often, but not always, coincide with periods of increased trade in poultry (e.g. lunar new year festivals), cooler weather conducive to survival of influenza viruses, and, in some places, wild bird movements. Surveillance studies help to determine the level of threat but capacity in most countries is not sufficient to quantify this at all times for all places. This is also influenced by the control measures used to prevent further losses. Long term trends in disease prevalence are needed to draw conclusions about the current state of the disease.

Genetic studies of recent (2006) H5N1 HPAI isolates demonstrate that, as expected for influenza A viruses, these viruses are evolving through both reassortment and point mutations. New genotypes continue to emerge as they have over the previous 10 years. Considerable variation is occurring within existing HA subclades (e.g. the evolution of viruses in Europe and Africa (Salzberg et al 2007)) and antigenic variants and new clades have also been described, including one in Shanxi province in China that required development and introduction of a vaccine based around this antigen. This strain of virus (A/chicken/Shanxi/2/2006) was causing clinical disease in vaccinated layers.

There are significant gaps in the genetic data, which makes it appear as if some new strains emerge *de novo*. This demonstrates the imperfections in current surveillance systems as well as demonstrating the continuing evolution of these viruses (see WHO 2007 for a phylogenetic tree demonstrating relationships between recent isolates).

¹ According to FAO's classification system

² Discussed in a presentation by Anmarie Bouma at an international seminar on vaccination held in Jakarta from 11-12 June 2007.

Clade 1 viruses, which were first detected in Vietnam and Thailand in 2004, continue to circulate in southern Vietnam and have been found in cases in Thailand in 2006 indicating they have not been eradicated from this region.

Viruses in Indonesia (sub-clade 2.1) have diverged into a number of sublineages (Smith et al 2006b). Somewhat surprisingly there have been no detections of these Indonesian (sub-clade 2.1) viruses in other countries or additional introductions of other H5N1 viruses to Indonesia since these were first introduced to the country in 2003.

All viruses detected north west of Myanmar (apart from those detected by quarantine officials in traded/smuggled wild birds in the UK and Belgium) appear to belong to WHO subclade 2.2 – the sub-clade that was initially found in dead wild birds in Qinghai in 2005. These sub-clade 2.2 viruses have continued to evolve, forming further distinct sub-lineages within this sub-clade (Salzberg et al 2007).

Sub-clade 2.3 viruses have now been detected in a range extending from Malaysia to China.

Based on experiences over the past 10 years, a number of factors have been identified that assist in assessing whether a particular country is at high risk of developing entrenched infection, after virus incursion, despite the efforts of veterinary services to control it. These factors are large numbers of concentrated commercial farms with poor biosecurity conditions; large numbers of smallholder producers; large numbers of traders and middlemen selling poultry through poorly controlled live bird markets; large populations of free grazing or pond ducks; inadequate law enforcement, and weak veterinary services.

Where these conditions exist, traditional control measures, based around stamping out and movement controls, have not been successful in eliminating infection. In such cases, early use of other measures to bring down the levels of infection, especially vaccination, before embarking on eradication campaigns is justified.

Apart from Egypt and Indonesia, reports of human cases have largely ceased or occur sporadically, following the progressive control of H5N1 HPAI in poultry³. This achievement is arguably the most important demonstration of the effects of worldwide efforts to contain these viruses.

Epidemiological analyses of this disease are still hampered by the quality of surveillance data and disease investigations. There is considerable unreported infection in poultry in countries or parts of countries where surveillance is weak. This was, on some occasions, demonstrated by the occurrence of human cases of this zoonotic disease in places where disease or infection has not been reported in poultry. Some of this could also be due to sub-clinical infections in ducks and to poultry incubating disease in live poultry markets but slaughtered before disease becomes apparent. Surveillance in vaccinated areas has to be intensified in order to detect any circulation and/or changes of the virus or possible changes in disease expression.

Wild birds were strongly implicated as the most likely source of viruses for scattered outbreaks of disease in poultry in Europe in 2006, although not all avian species responsible for introducing the viruses are known. Multiple virus introductions are suspected in Africa (Salzberg et al 2007).

³ The true infection rate in humans is not fully documented. Nevertheless the reported number of human cases provides an independent, crude assessment of the levels of infection in poultry.

Deaths of wild bird from H5N1 HPAI occurred in 2005 especially in autumn and summer in Russia and China, and again in 2006, but with fewer reported cases. So far, in the second quarter of 2007 only Hong Kong SAR has reported dead infected free flying birds, which could be related to trade in song birds rather than migration. This absence of reported cases in north- western China and Russia in 2007 may indicate that infection in wild birds is continuing to decline, although annual seasonal effects, sub-clinical infections and possible under-reporting need to be taken into account.

H5N1 HPAI viruses have been detected rarely in live wild birds. Surveillance studies on wild birds, as conducted in Europe, demonstrate that if H5N1 HPAI viruses are present in normal populations of these birds this must be at very low levels.

Experiences over the past few years demonstrate the difficulties in predicting the behaviour of H5N1 viruses. Gains will continue to be made locally in controlling this disease but global eradication of the viruses remains a distant and unlikely prospect as long as high risk production and marketing practices persist in places with entrenched infection and as long as surveillance and early response systems do not improve dramatically through strengthening of veterinary services and extensive private-public partnerships.

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