

## **SCIENTIFIC SUMMARY OF HIGHLY PATHOGENIC AVIAN INFLUENZA H5N1: WILDLIFE AND CONSERVATION CONSIDERATIONS**

### **Definition of avian influenza**

Avian influenza is a highly contagious disease caused by influenza A viruses, affecting many species of birds. Avian influenza is classified according to disease severity into two recognised forms: low pathogenic avian influenza (LPAI) and highly pathogenic avian influenza (HPAI). LPAI viruses are generally of low virulence, while HPAI viruses are highly virulent in most poultry species resulting in nearly 100% mortality in infected domestic flocks (Center for Infectious Disease Research & Policy 2007). The natural reservoir of LPAI viruses is in wild waterbirds – most commonly in ducks, geese, swans, waders/shorebirds and gulls (Hinshaw & Webster 1982; Webster *et al.* 1992; Stallknecht & Brown 2007).

To date, influenza A viruses representing 16 haemagglutinin (HA) and nine neuraminidase (NA) subtypes have been described in wild birds and poultry throughout the world (Rohm *et al.* 1996; Fouchier *et al.* 2005). Viruses belonging to the antigenic subtypes H5 and H7, in contrast to viruses possessing other HA subtypes, may become highly pathogenic having been transmitted in low pathogenic form from wild birds to poultry and subsequently circulating in poultry populations (Senne *et al.* 1996).

Notifiable avian influenza is defined by the World Organisation for Animal Health (OIE) as "an infection of poultry caused by any influenza A virus of the H5 or H7 subtypes or by any avian influenza virus with an intravenous pathogenicity index (IVPI) greater than 1.2 (or as an alternative at least 75% mortality)" as described by the OIE's Terrestrial Animal Health Code (OIE 2007).

### **Genesis of highly pathogenic avian influenza viruses**

In wild waterbirds, LPAI viruses are a natural part of the ecosystem. They have been isolated from over 90 species of wild bird (Stallknecht & Shane 1988, Olsen *et al.* 2006; Lee 2008), and are thought to have existed alongside wild birds for millennia in balanced systems. In their natural hosts, avian influenza viruses infect the gastro-intestinal tract and are shed through the cloaca; they generally do not cause disease although some behavioural anomalies have been reported, such as reduced migratory and foraging performance in Bewick's Swans *Cygnus columbianus bewickii* (van Gils *et al.* 2007); instead, the viruses remain in evolutionary stasis as indicated by low genetic mutation rates (Gorman *et al.* 1992; Taubenberger *et al.* 2005).

When LPAI viruses are transmitted to vulnerable poultry species, only mild symptoms such as a transient decline in egg production or reduction in weight gain (Capua & Mutinelli 2001) are induced. However, where a dense poultry environment supports several cycles of infection, the viruses may mutate, adapting to their new hosts, and for the H5 and H7 subtypes these mutations can lead to generation of a highly pathogenic form. Thus, HPAI viruses are essentially products of intensively farmed poultry, and their incidence has increased dramatically with the greatly enhanced volume of poultry production around the world (GRAIN 2006; Greger 2006). In the first few years of the 21<sup>st</sup> century the incidence of HPAI outbreaks has already exceeded the total number of outbreaks recorded for the entire 20<sup>th</sup> century (Greger 2006). In general, they should be viewed as something artificial, made possible by intensive poultry production techniques.

After an HPAI virus has arisen in poultry, it has the potential both to re-infect wild birds and to cause disease in various mammalian taxa. If influenza A viruses adapt inside these new hosts to become highly transmissible, there can be devastating consequences, such as the human influenza pandemics of the 20th century (Kilbourne 2006). The conditions necessary for cross-infection are provided by agricultural practices that bring together humans, poultry and other species in high densities in areas where there is also the potential for viral transmission from infected poultry, poultry products and waste to wild birds, humans and other mammals in shared wetlands and in 'wet' (*i.e.* live animal) markets (Shortridge 1977; Shortridge *et al.* 1977).

## Highly pathogenic avian influenza H5N1 of Asian lineage (HPAI H5N1)

HPAI H5N1 of Asian lineage has infected domestic, captive and wild birds in more than 60 countries in Asia, Europe and Africa (OIE 2008). By November 2005, i.e. before widespread occurrence in western Eurasia and Africa, over 200 million domestic birds had died from the disease or been slaughtered in attempts to control its spread; the economies of the worst affected countries in southeast Asia have suffered greatly, with lost revenue estimated at over \$10 billion (Diouf 2005), and there have been serious human health consequences. By March 2008, the World Health Organisation had confirmed more than 370 human cases, over 60% of those fatal (World Health Organisation 2008).

Sporadic deaths in wild birds have been reported since 2002 and the first outbreak involving a large number of wild birds was reported in May 2005, in Qinghai province, China (Chen *et al.* 2005; Liu *et al.* 2005). Between 2002 and the present, the virus has infected a wide range of wild bird species (Olsen *et al.* 2006; USGS National Wildlife Health Center 2008; Lee 2008), but which species are important in H5N1 HPAI movement and whether the virus will become enzootic in wild bird populations is still unknown (Brown *et al.* 2006).

The virus has also infected a limited number of domestic, captive and wild mammals, including captive Tigers *Panthera tigris* and Leopards *Panthera pardus* and domestic pigs in southeast Asia, and domestic cats and a wild Stone Marten *Martes foina* in Germany. These cases were the result of 'spillover' infection from birds. There is no known reservoir of HPAI H5N1 virus in mammals and there remains no sound evidence that the virus can be readily transmitted from mammal to mammal.

## Emergence of HPAI H5N1 in poultry in southeast Asia (1996 – 2005)

HPAI H5N1 first received widespread recognition following a 1997 outbreak in poultry in Hong Kong SAR with subsequent spread of the virus to humans. During that outbreak, 18 human cases were recognised and six patients died. The outbreak ended when all domestic chickens held by wholesale facilities and vendors in Hong Kong were slaughtered (Snacken 1999). A precursor to the 1997 H5N1 strain was identified in Guangdong, China, where it caused deaths in domestic geese in 1996 (Webster *et al.* 2006).

Between 1997 and 2002, different reassortments (known as genotypes) of the virus emerged, in domestic goose and duck populations, which contained the same H5 HA gene but had different internal genes (Guan *et al.* 2002; Webster *et al.* 2006).

In 2002, a single genotype emerged in Hong Kong SAR and killed captive and wild waterbirds in nature parks there. This genotype spread to humans in Hong Kong in February 2002 (infecting two, killing one) and was the precursor to the Z genotype that later became dominant (Sturm-Ramirez *et al.* 2004; Ellis *et al.* 2004).

Between 2003 and 2005, the Z genotype spread in an unprecedented fashion across southeast Asia, affecting domestic poultry in Vietnam, Thailand, Indonesia, Cambodia, Laos, Korea, Japan, China and Malaysia. Later analysis showed that the H5N1 viruses that caused outbreaks in Japan and Korea were genetically different from those in other countries (the V genotype) (Mase *et al.* 2005; Li *et al.* 2004; Webster *et al.* 2006).

In April 2005, the first major outbreak in wild birds was reported. Some 6345 wild birds were reported dead at Qinghai Lake in central China. Species affected included Great Black-headed Gull *Larus ichthyaetus*, Bar-headed Goose *Anser indicus*, Brown-headed Gull *Larus brunnicephalus*, Great Cormorant *Phalacrocorax carbo* and Ruddy Shelduck *Tadorna ferruginea* (Chen *et al.* 2005; Liu *et al.* 2005).

## Geographical spread of HPAI H5N1 out of southeast Asia (2005 – 2006)

In July 2005, Russia reported its first outbreaks; domestic flocks were affected in six regions of western Siberia and dead wild birds were reported in the vicinities of some of these outbreaks.

Kazakhstan reported its first outbreak in August 2005 in domestic birds. In the same month, 89 wild birds described as migratory species were reported infected at two lakes in Mongolia.

Europe reported its first outbreaks in October 2005 when infection was detected in domestic birds in Romania and Turkey. In the same month, Romania reported sporadic cases in wild birds as did Croatia and European parts of Russia. In November, the virus spread to domestic birds in the Ukraine, and the Middle East reported its first case: a flamingo kept as a captive bird in Kuwait. During December, two outbreaks were reported in European Russia in wild swans (species unreported) in regions near the Caspian Sea.

In the first half of 2006, the spread of HPAI H5N1 continued across Europe (Sabirovic *et al.* 2006; Hesterberg *et al.* 2007) and the Middle East and into Africa. Between January and May, infection was reported in 24 European countries with the majority of cases occurring in February and March in wild birds. During the same period, outbreaks were reported across central Asia and the Middle East, affecting domestic birds in Azerbaijan, India, Bangladesh, Pakistan, Iran and Iraq, with Azerbaijan also reporting infected wild birds. The first reported outbreak in Africa occurred in January in poultry in Nigeria, and by the end of April, eight other African nations had reported outbreaks: Burkina Faso, Cameroon, Djibouti, Egypt, Ghana, the Ivory Coast, Niger and Sudan (OIE 2008).

By May 2006, reports of outbreaks in Europe, the Middle East and Africa had for the most part decreased in frequency. Small numbers of cases of infection were reported in Hungary, Spain and the Ukraine in June; Pakistan and Russia in July; and one case was identified in a captive swan in Germany in August. Egypt was exceptional, continuously reporting outbreaks throughout 2006. It is also considered likely that outbreaks continued in poultry in Nigeria (UN System Influenza Coordinator & World Bank 2007).

Throughout the time HPAI H5N1 was spreading across central Asia, Europe, the Middle East and Africa, it maintained a stronghold in poultry in southeast Asia. In 2006, outbreaks were reported in Cambodia, China, Hong Kong, Indonesia, Korea, Laos, Malaysia, Myanmar, Thailand and Vietnam (OIE 2008).

### **Outbreaks of HPAI H5N1 since 2006 and the current situation**

Compared with 54 countries reporting 1,470 outbreaks to the OIE in 2006, 30 countries reported 638 outbreaks in 2007 (OIE 2008). In 2007, six European countries (Poland, Hungary, Germany, the United Kingdom, Romania and the Czech Republic) reported sporadic and relatively isolated outbreaks in poultry that were quickly controlled. Outbreaks in domestic birds were also reported in European parts of Russia and in Turkey. Infected wild birds were reported in Germany, France, the United Kingdom and the Czech Republic; and birds at a rehabilitation centre were affected in Poland. In the Middle East and central Asia, poultry outbreaks occurred throughout 2007. Some 350 outbreaks were reported from Egypt and Bangladesh alone. Poultry (and in some cases captive birds) were also affected in India, Kuwait, Saudi Arabia, Pakistan, Afghanistan and Israel with most outbreaks occurring between February and April, and again between October and December. In Africa, HPAI H5N1 was reported in domestic birds in Togo, Ghana and Benin; and is considered to have become enzootic in Nigeria (OIE 2008; UN System Influenza Coordinator & World Bank 2007). Again, as in 2006, poultry outbreaks continued across southeast Asia. Sporadic cases in wild birds were reported in Japan and Hong Kong SAR.

In January and February 2008, a small number of wild bird cases were detected in the United Kingdom; large numbers of poultry outbreaks occurred in India and parts of southeast Asia; and the virus was considered to be enzootic in poultry in Egypt, Indonesia and Nigeria; and possibly enzootic in Bangladesh and China (UN System Influenza Coordinator & World Bank 2007).

## Major outbreaks of HPAI H5N1 in wild birds

Prior to HPAI H5N1, reports of HPAI in wild birds were very rare. The broad geographical scale and extent of the disease in wild birds is both extraordinary and unprecedented. The following table (Table 1) summarises the known major outbreaks of HPAI H5N1 in wild birds.

Table 1. Major known outbreaks of highly pathogenic avian influenza H5N1 in wild birds\*

Year	Month(s)	Location(s)	Description of affected birds
2005	April	Qinghai Lake in central China	6345 waterbirds, the majority of which were Great Black-headed Gulls <i>Larus ichthyaetus</i> , Bar-headed Geese <i>Anser indicus</i> and Brown-headed Gulls <i>Larus brunnicephalus</i>
	August	Lake Erhel & Lake Khunt in Mongolia	89 waterbirds including ducks, geese and swans
	October – November	Romania & Croatia	Over 180 waterbirds, mainly swans
2006	January	Coastal area in the vicinity of Baku, Azerbaijan	Unspecified number of birds reported to the OIE as “various migratory birds”
	January – May	23 countries in Europe including Turkey and European Russia	Most cases occurred in ducks, geese and swans but a wide variety of species was infected including other waterbirds and raptors
	February	Rasht, Iran	153 wild swans
	May	Multiple locations in Qinghai province, China	Over 900, mainly waterbirds, and mostly Bar-headed Geese <i>Anser indicus</i>
	May	Naqu, Tibet	Over 2,300 birds – species composition unclear but 300 infected Bar-headed Geese <i>Anser indicus</i> were reported
	June	Lake Hunt in Bulgan, Mongolia	Twelve waterbirds including swans, geese and gulls
2007	June	Germany, France and the Czech Republic	Over 290, mainly waterbirds, found mostly in Germany

\* Data sources include OIE disease information reports and the German Friedrich-Loeffler Institute epidemiological bulletins – dates, locations and numbers may differ slightly in other sources.

Numerous species of wild birds, especially waterbirds, are susceptible to infection by the HPAI H5N1 virus. Close contact between poultry and wild birds can lead to cross-infection, from poultry to wild birds and from wild birds to poultry. Additionally, species that live in and around poultry farms and human habitations may serve as “bridge species” that could potentially transmit the virus between poultry and wild birds either by direct contact between wild birds and poultry kept outside or by indirect contact with contaminated materials. While there is no sound evidence that wild birds have carried the virus long distances on migration (Feare & Yasué 2006), analysis of genetic sequences and other largely indirect evidence suggests that wild birds are likely to have contributed to spread (Chen *et al.* 2006; Keawcharoen *et al.* 2008; Kilpatrick *et al.* 2006; Hesterberg *et al.* 2007; Weber & Stilianakis 2007). The relative importance of different modes of infection transfer, however, is unclear in the present state of knowledge.

Poor planning in response to development pressures has led to the increasing loss or degradation of wild ecosystems, which are the natural habitats for wild birds. This has resulted in closer contact between wild populations, domesticated birds such as chickens, ducks, geese, and other domestic fowl, and humans and has thus provided greater opportunities for the spread of HPAI H5N1 between wild and domestic birds, and thence to humans. The interplay between agriculture, animal (domestic and wild) health, human health, ecosystem health, and socio-cultural factors has been important in the emergence and spread of the virus.

### **Avian influenza and wetlands**

Given the ecology of the natural hosts of LPAI viruses, it is unsurprising that wetlands play a major role in the natural epidemiology of avian influenza. As with many other viruses, avian influenza virions survive longer in colder water (Lu *et al.* 2003; Stallknecht *et al.* 1990), and the virus is strongly suggested to survive over winter in frozen lakes in Arctic and sub-Arctic breeding areas. Thus, as well as the waterbird hosts, these wetlands are probably permanent reservoirs of LPAI virus (Rogers *et al.* 2004; Smith *et al.* 2004) (re-)infecting waterbirds arriving from southerly areas to breed (shown in Siberia by Okazaki *et al.* 2000 and Alaska by Ito *et al.* 1995). Indeed, in some wetlands used as staging grounds by large numbers of migratory ducks, avian influenza viral particles can be readily isolated from lake water (Hinshaw *et al.* 1980).

An agricultural practice that provides ideal conditions for cross-infection and thus genetic change is used on some fish-farms in Asia: battery cages of poultry are placed directly over troughs in pig-pens, which in turn are positioned over fish farms. The poultry waste feeds the pigs, the pig waste is either eaten by the fish or acts as a fertiliser for aquatic fish food, and the pond water is sometimes recycled as drinking water for the pigs and poultry (Greger 2006). These kinds of agricultural practices afford avian influenza viruses, which are spread via the faecal-oral route, a perfect opportunity to cycle through a mammalian species, accumulating the mutations necessary to adapt to mammalian hosts. Thus, as the use of such practices increases, so does the likelihood that new influenza strains infectious to and transmissible between humans will emerge (Culliton 1990; Greger 2006).

As well as providing conditions for virus mutation and generation, agricultural practices, particularly those used on wetlands, can enhance the ability of a virus to spread. The role of Asian domestic ducks in the epidemiology of HPAI H5N1 has been closely researched and found to be central not only to the genesis of the virus (Hulse-Post *et al.* 2005; Sims 2007), but also to its spread and the maintenance of infection in several Asian countries (Shortridge & Melville 2006). Typically this has involved flocks of domestic ducks used for 'cleaning' rice paddies of waste grain and various pests, during which they can potentially have contact with wild ducks using the same wetlands. Detailed research (Gilbert *et al.* 2006; Songserm *et al.* 2006) in Thailand has demonstrated a strong association between the HPAI H5N1 virus and abundance of free-grazing ducks. Gilbert *et al.* (2006) concluded that in Thailand "wetlands used for double-crop rice production, where free-grazing duck feed year round in rice paddies, appear to be a critical factor in HPAI persistence and spread".

### **Wildlife conservation implications**

Prior to HPAI H5N1, reports of HPAI in wild birds were very rare. The broad geographical scale and extent of the disease in wild birds is both extraordinary and unprecedented, and the conservation impacts of HPAI H5N1 have been significant.

It is estimated that between 5-10% of the world population of Bar-headed Goose *Anser indicus* died at Lake Qinghai, China in spring 2005 (Chen *et al.* 2005; Liu *et al.* 2005). At least two globally threatened species have been affected: Black-necked Crane *Grus nigricollis* in China and Red-breasted Goose *Branta ruficollis* in Greece. Approximately 90% of the world population of Red-breasted Goose is confined to just five roost sites in Romania and Bulgaria, countries that have both reported outbreaks, as also have Russia and Ukraine where they also over-winter (BirdLife International 2007).

However, the total number of wild birds known to have been affected has been small in contrast to the number of domestic birds affected, and many more wild birds die of commoner avian diseases each year. Perhaps a greater threat than direct mortality has been the development of public fear about waterbirds resulting in misguided attempts to control the disease by disturbing or destroying wild birds and their habitats. Such responses are often encouraged by exaggerated or misleading messages in the media.

Currently, wildlife health problems are being created or exacerbated by unsustainable activities such as habitat loss or degradation, which facilitates closer contact between domestic and wild animals. Many advocate that to reduce risk of avian influenza and other bird diseases, there is a need to move to markedly more sustainable systems of agriculture with significantly lower intensity systems of poultry production. These need to be more biosecure, separated from wild waterbirds and their natural wetland habitats resulting in far fewer opportunities for viral cross-infection and thus pathogenetic amplification (Greger 2006). There are major animal and human health consequences (in terms of the impact on economies, food security and potential implications of a human influenza pandemic) of not strategically addressing these issues. However, to deliver such an objective in a world with an ever-growing human population and with issues of food-security in many developing countries, will be a major policy challenge.

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