

Avian influenza infections in birds – a moving target

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Avian influenza (AI) is a complex infection of birds, of which the ecology and epidemiology have undergone substantial changes over the last decade. Avian influenza viruses infecting poultry can be divided into two groups. The very virulent viruses cause highly pathogenic avian influenza (HPAI), with flock mortality as high as 100%. These viruses have been restricted to subtypes H5 and H7, although not all H5 and H7 viruses cause HPAI. All other viruses cause a milder, primarily respiratory, disease (low pathogenic avian influenza, LPAI), unless exacerbated by other infections or environmental conditions. Until recently, HPAI viruses were rarely isolated from wild birds, but for LPAI viruses extremely high isolation rates have been recorded in surveillance studies, particularly in feral waterfowl. In recent years, there have been costly outbreaks of HPAI in poultry in Italy, the Netherlands and

Canada and in each of these countries millions of birds were slaughtered to bring the outbreaks under control. However, these outbreaks tend to have been overshadowed by the H5N1 HPAI virus, initially isolated in China, that has now spread in poultry and/or wild birds throughout Asia and into Europe and Africa, resulting in the death or culling of hundreds of millions of poultry and posing a significant zoonosis threat. Since the 1990s, AI infections due to two subtypes, LPAI H9N2 and HPAI H5N1, have been widespread in poultry across large areas of the world, resulting in a modified eco-epidemiology and a zoonotic potential. An extraordinary effort is required to manage these epidemics from both the human and animal health perspectives.

Keywords Avian influenza, epidemiology, recent changes.

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Introduction

In the last 10 years, many aspects of the epidemiology of avian influenza (AI) infections in poultry and other birds appear to have changed dramatically from those established in the preceding century. The number of outbreaks of the highly pathogenic avian influenza (HPAI) disease has increased alarmingly in the last 10 years and, even more noticeably, the impact in terms of the number of birds involved and the costs of disease control have dramatically escalated. But what has been most notable is the apparently unprecedented emergence and spread of the HPAI H5N1 virus in south-east Asia and beyond which, with the zoonotic infections have resulted in AI being considered one of the most important animal diseases, if not the most important. In this article, the conventional and changing epidemiology of AI is reviewed.

Aetiology

Influenza viruses have segmented, negative sense, single-strand RNA genomes and are placed in the family *Ortho-*

myxoviridae. At present, the *Orthomyxoviridae* family consists of five genera; only viruses of the *Influenzavirus A* genus are known to infect birds.

Influenza A viruses are further divided into subtypes based on the antigenic relationships in the surface glycoproteins, haemagglutinin (HA) and neuraminidase (NA). At present, 16 HA subtypes (H1–H16) and nine NA subtypes (N1–N9) have been recognized. Each virus has one HA and one NA antigen, apparently in any combination. All influenza A subtypes in the majority of possible combinations have been isolated from avian species. To date, only viruses of H5 and H7 subtype have been shown to cause HPAI in susceptible species, but not all H5 and H7 viruses are virulent.

For all influenza A viruses, the haemagglutinin glycoprotein is produced as a precursor, HA0, which requires post-translational cleavage by host proteases before it is functional and virus particles are infectious.¹ The HA0 precursor proteins of AI viruses of low virulence for poultry (low pathogenic avian influenza, LPAI viruses) have a single arginine at the cleavage site and another basic amino acid at position –3 or –4 from the cleavage site. These viruses are

limited to cleavage by extracellular host proteases such as trypsin-like enzymes and thus restricted to replication at sites in the host where such enzymes are found, i.e. the respiratory and intestinal tracts. Highly pathogenic avian influenza viruses possess multiple basic amino acids (arginine and lysine) at their HA0 cleavage sites as a result of either apparent insertion or apparent substitution²⁻⁴ and appear to be cleavable by an intracellular ubiquitous protease(s), probably one or more proprotein-processing subtilisin-related endoproteases of which furin is the leading candidate.⁵ Highly pathogenic avian influenza viruses are able to replicate throughout the bird, damaging vital organs and tissues, which results in disease and death.

To date, only viruses of the H5 and H7 subtypes have been shown to cause HPAI. It appears that HPAI viruses arise by mutation after LPAI viruses have been introduced into poultry. Several mechanisms appear to be responsible for this mutation. Most HPAI viruses appear to have arisen as a result of spontaneous duplication of purine triplets which results in the insertion of basic amino acids at the HA0 cleavage site and this occurs due to a transcription fault by the polymerase complex.⁶ However, as pointed out by Perdue *et al.*⁶ this is clearly not the only mechanism by which HPAI viruses arise as some appear to result from nucleotide substitution rather than insertion, while others have insertions without repeating nucleotides. The Chile 2002⁷ and the Canada 2004⁸ H7N3 HPAI viruses show distinct and unusual cleavage site amino acid sequences. These viruses appear to have arisen as a result of recombination with other genes (nucleoprotein gene and matrix gene, respectively) resulting in an insertion at the cleavage site of 11 amino acids for the Chile virus and seven amino acids for the Canadian virus.

The factors that bring about mutation from LPAI to HPAI are not known. In some instances, mutation seems to have taken place rapidly (at the primary site) after introduction from wild birds, in others the LPAI virus has circulated in poultry for months before mutating. Therefore, it is impossible to predict if and when this mutation will occur. However, it can be reasonably assumed that the wider the circulation of LPAI in poultry, the higher the chance that mutation to HPAI will occur.

Highly pathogenic avian influenza viruses are not necessarily virulent for all species of birds and the clinical severity seen in any host appears to vary with both bird species and virus strain.^{9,10} In particular, ducks rarely show clinical signs as a result of HPAI infections, although there are reports that some of the Asian H5N1 viruses have caused disease¹¹ and the HPAI viruses A/duck/Italy/2000 (H7N1) and A/chicken/Germany/34 (H7N1) have been reported to cause disease and death in naturally and experimentally infected waterfowl.¹²

Host range

Influenza viruses have been shown to infect a great variety of birds (for reviews see Refs 13–17) including free-living birds, captive-caged birds, domestic ducks, chickens, turkeys and other domestic poultry.

It was not until the mid-1970s that any systematic investigations of influenza in feral birds were undertaken. These investigations revealed enormous pools of influenza viruses to be present in the wild bird population^{17–20} especially in waterfowl, family Anatidae, order Anseriformes. In the surveys listed by Stallknecht and Shane,¹⁹ a total of 21 318 samples from all species resulted in the isolation of 2317 (10.9%) viruses. However, 14 303 of these samples were from birds of the order Anseriformes which yielded 2173 (15.2%) isolates. The next highest isolation rates were 2.9% and 2.2% from the Passeriformes and Charadriiformes, respectively, but these compare with an overall isolation rate of 2.1% from all birds other than ducks and geese. However, studies by Sharp *et al.*²¹ suggest that waterfowl do not act as a reservoir for all avian influenza viruses. It seems likely that part of the influenza gene pool is maintained in shorebirds and gulls, from which the predominant number of isolated influenza viruses are of a different subtype to those isolated from the ducks.²²

Until the spread of Asian HPAI H5N1 (see below), HPAI viruses had been isolated rarely from free-living birds and, apart from A/tern/South Africa/61,²³ when they had been isolated, it was usually in the vicinity of outbreaks of HPAI in poultry or geographically and chronologically close to known outbreaks in poultry.

Transmission

The mechanisms by which influenza viruses pass from one bird to another and bring about infection are poorly understood. Results of experiments to assess the transmissibility of LPAI and HPAI viruses in domestic poultry^{10,12,24–26} have indicated that bird-to-bird transmission is extremely complex and depends on the strain of virus, the species of bird and environmental factors.

The different epidemiology of the Asian H5N1 HPAI has led to several groups re-examining the understanding of AI virus transmission. In particular, the change in the primary route of transmission from faecal/oral to the respiratory route in land birds, especially minor poultry species such as quail and pheasants, has been considered significant in the epidemiology of that virus, especially in its spread to mammals.^{27–29}

Spread

Until recently, it appeared that the epidemiology of AI consisted of the perpetuation of LPAI viruses of all H subtypes

in wild birds, where they caused little or no disease, with spread from time to time to poultry. Very occasionally, introductions of LPAI viruses of H5 or H7 subtype into poultry resulted in the mutation of these viruses to virulent viruses that caused HPAI.

The degree to which LPAI or HPAI viruses occur and spread in poultry appears to be considerably variable and to depend on the levels of biosecurity and concentration of poultry in the vicinity of the initial outbreaks or the emergence of HPAI virus. Since the late 1990s and especially after 2003, events occurred that completely changed our concepts of AI epidemiology and the spread of LPAI virus of H9N2 subtype and HPAI virus of H5N1 subtype need separate consideration from the more conventional situation.

Conventional situation

Primary introduction to poultry

In the conventional situation, the primary introduction of LPAI viruses into a poultry population occurs as a result of wild bird activity, usually waterfowl. This may not necessarily involve direct contact as infected waterfowl may take the viruses to an area and these may then be introduced to poultry by humans, other types of birds or other animals, which do not need to be infected but may transfer the virus mechanically in infective faeces from the waterfowl. Surface water used for drinking may also be contaminated with AI viruses and a source of infection. There is much evidence implicating waterfowl in the vast majority of primary LPAI outbreaks as: (i) there is a much higher prevalence of infection of poultry on migratory waterfowl routes although in view of the variation in virus excretors along the flyways³⁰ this may occur more frequently at some stages of the migratory route than others, e.g. Minnesota, USA compared with other states on the Mississippi flyway;³¹ (ii) there is a higher prevalence of infection of poultry kept in exposed conditions (e.g. turkeys on range and ducks on fattening fields) and, conversely, where there have been regular LPAI infections and change to a policy of confinement has been pursued LPAI problems largely disappear;^{32,33} (iii) surveillance studies in areas with LPAI problems in poultry have shown the same variation in virus subtypes in sampled waterfowl and turkey outbreaks;³⁴ (iv) influenza outbreaks show a seasonal occurrence in high-risk areas, which coincides with migratory activity;^{35,36} (v) in most documented specific outbreaks, evidence has been obtained of probable waterfowl contact at the initial site.

On some occasions, primary introduction to poultry has resulted from a sector where AI virus may be endemic, for example, the H7N2 LPAI outbreaks in the USA.³⁶ Low pathogenic avian influenza virus of H7N2 subtype appears to have been introduced into the live bird markets in the

eastern USA in 1994 and despite attempts to eradicate the virus it has remained endemic since then. Senne *et al.*³⁷ report that in the last 10 years eight LPAI H7N2 outbreaks in commercial poultry, resulting in the slaughter of millions of birds and severe economic losses have been linked to the live bird markets.

Secondary spread

The greatest threat of spread of avian influenza viruses is by mechanical transfer of infective faeces, in which virus may be present at concentrations as high as 10^7 infectious particles/gram and may survive for longer than 44 days.³⁸ Birds or other animals that are not themselves susceptible to infection may become contaminated and spread the virus. Shared water or food may also become contaminated. However, for domestic poultry, the main source of secondary spread appears to be humans. In several specific accounts, strong evidence has implicated the movements of caretakers, farm owners and staff, trucks and drivers moving birds or delivering food and artificial inseminators in the spread of the virus both on to and through a farm.^{39–41}

Spread by personnel and fomites was the method most strongly suspected in the widespread and devastating epizootic in chickens in Pennsylvania during 1983–1984. Although there was some evidence that windborne spread might have played a role amongst very closely situated farms and that flying insects could become contaminated with infected faeces, it was concluded by most observers that secondary spread was principally due to the movement of personnel and equipment between farms.^{38,42,43} King⁴³ listed six types of fomite that may be moved from farm to farm and 11 types of personnel who may be in contact with two farms or more; Utterback³⁸ produced even longer lists. In the more recent outbreaks, such as those in Italy in 1999–2000, the density of the poultry population in the infected area and the frequent contact between farms by feed trucks, abattoir trucks and other vehicles have been associated with the considerable spread of virus.⁴⁴

H9N2 virus

Historically, LPAI viruses have not been the subject of notification and control aimed at eradication and it was not clear why they had not become more ubiquitous and endemic in poultry across large geographical areas as had other viruses such as avian pneumoviruses or avian infectious bronchitis viruses. However, this is exactly what seems to have occurred with H9N2 LPAI viruses and infections of poultry, mainly chickens, have occurred in many countries since the mid-1990s and reached panzootic proportions. Outbreaks due to H9N2 AI occurred in domestic ducks, chickens and turkeys in Germany during 1995–1997, 1998 and 2004;^{44–46} in chickens in Italy in 1994 and 1996,⁴⁷ pheasants in Ireland in 1997,⁴⁸ ostriches in South Africa in

1995,⁴⁹ turkeys in the USA in 1995 and 1996⁵⁰ and in chickens in Korea in 1996.⁵¹ More recently, H9N2 infections have been reported in the Middle East and Asia causing widespread outbreaks in commercial chickens in Iran, Saudi Arabia, Pakistan, China, Korea, UAE, Israel, Jordan, Kuwait, Lebanon, Libya and Iraq.^{52,53} In several of these countries, vaccines have been deployed to bring the disease under control, but nevertheless it appears that H9N2 infections have become endemic in commercial poultry in a significant number of countries.

Asian HPAI H5N1 virus

The emergence of HPAI H5N1 virus in south-east Asia and its spread across Asia and into Europe are unprecedented in the virological era. The apparent progenitor virus for the subsequent outbreaks of HPAI of H5N1 subtype was obtained from an infection of commercial geese in Guangdong Province, PR China in 1996.⁵⁴ In some reports, it has been considered that the virus continued to circulate in southern China primarily in domestic ducks and showing some genetic variation.⁵⁵ This apparent low level, but probably endemic, situation changed dramatically during December 2003 to February 2004 when suddenly eight countries in east and south-east Asia reported outbreaks of HPAI due to H5N1 virus.⁵⁵ Although there seemed to be some success in controlling the outbreaks in some countries, it appeared to re-emerge in a second wave in July 2004 onwards. Malaysia reported an outbreak in poultry in August 2004 and became the ninth country in the region to be affected.⁵⁶ The virus appeared to affect all sectors of the poultry populations in most of these countries, but its presence in free range commercial ducks, village poultry, live bird markets and fighting cocks seemed especially significant in the spread of the virus.^{54,55,57}

If HPAI virus becomes widespread in poultry, especially in domestic ducks that are reared on free range, spillover into wild bird populations is inevitable. In the past, such infections have been restricted to wild birds found dead in the vicinity of infected poultry, but there has always been a concern that infections of wild birds in which HPAI virus caused minimal or no clinical signs (i.e. ducks) could result in spread of the virus over large areas and long distances. Outbreaks affecting many wild bird species at two waterfowl parks in Hong Kong were recorded in 2002⁵⁸ and further, possibly more significant, outbreaks in wild migratory birds were reported in China and Mongolia in 2005. In particular, it was suggested that the presence of virus in migratory birds at Lake Qinghai in western China could be the means by which the H5N1^{59,60} virus could spread to the West and the South.

There is no good evidence that wild birds were responsible for the introduction into Russia but HPAI H5N1 virus, genetically closely related to isolates obtained at Lake

Qinghai, reached poultry there in the summer of 2005. Whether the virus spread from there to other west Asian and some east European countries or the virus was introduced independently is not clear, nor is whether the spread was associated with movements of poultry or wild birds. Probably both were involved, but during 2005 and up to the beginning of 2006 genetically closely related H5N1 viruses appeared in a number of countries in the region.

Reports of HPAI H5N1 virus infections continued in the first 3 months of 2006 and by early April 2006, 31 countries from Asia, Europe and Africa had reported HPAI caused by H5N1 virus to the World Organisation for Animal Health (OIE) since the end of 2003.⁵⁶

Two isolated incursions of HPAI H5N1 virus into Europe occurred in 2004 and 2005 and are good examples of the influence of humans in the potential spread of AI viruses. The first was detected when eagles smuggled from Thailand and confiscated at Brussels Airport, Belgium were shown to be infected with H5N1 virus genetically similar to those isolated in Thailand.⁶¹ The second when investigations of deaths in captive-caged birds held in quarantine in England, ostensibly from Taiwan, showed them to be as a result of HPAI H5N1 infection.⁶² In this case, the virus was genetically closest to the viruses isolated in China.

Isolates of Asian HPAI H5N1 were obtained from dead swans in Croatia in October 2005⁵⁶ and then during January to April 2006 wild mute swans or other wild birds were shown to be infected in Azerbaijan, Iran, Kazakhstan, Georgia and 20 European countries. It seems likely that mute swans, or other birds, over-wintering on the Black Sea became infected at a time when adverse weather conditions made the Black Sea inhospitable and the birds dispersed to other areas. However, this would not explain the appearance of apparently the same H5N1 strain in swans and wild birds on the Baltic Coast at the same time.

Occurrence of HPAI outbreaks

The outbreaks of HPAI in poultry since 1959 (when the first known HPAI outbreak caused by virus of H5 subtype occurred) are listed in Table 1. If the Asian H5N1 outbreaks are considered to be a single epizootic, there have been 24 or 23 (if the Hong Kong 1997 outbreak is considered to be part of the Asian H5N1 epizootic) outbreaks or epizootic in that time. In the first 20 years of the 47-year period (1959–1978), there were five outbreaks (frequency 5.0 years). In the next 20 years, there were 13 (frequency 1.54 years), while in the last 7 years (1999–2006), there have been seven outbreaks (frequency 1.0 years), including the unprecedented spread of the Asian H5N1 virus. Perhaps even more alarming than the increase in HPAI outbreaks is the number of birds affected. While in the first 12 outbreaks only one (Pennsylvania 1983) had resulted in

Table 1. Reported highly pathogenic avian influenza (HPAI) primary outbreaks in poultry* since 1959

HPAI virus causing outbreak(s)	Subtype	Approximate numbers of poultry involved	Extent of spread
1 A/chicken/Scotland/59	H5N1	Not known	One small farm
2 A/turkey/England/63	H7N3	29 000	Three small farms
3 A/turkey/Ontario/7732/66	H5N9	8000	One farm
4 A/chicken/Victoria/76	H7N7	58 000	One chicken farm, duck farm with LPAI H7N7 slaughtered
5 A/chicken/Germany/79	H7N7	Not known	One chicken farm, one goose farm
6 A/turkey/England/199/79	H7N7	9000	Three small farms
7 A/chicken/Pennsylvania/1370/83	H5N2	17 000 000	356 farms HPAI plus 90 LPAI or H5 antibodies
8 A/turkey/Ireland/1378/83	H5N8	307 000	Three farms (turkeys/chickens), one duck farm (270 000 ducks)
9 A/chicken/Victoria/85	H7N7	120 000	One farm
10 A/turkey/England/50-92/91	H5N1	8000	One house on one farm
11 A/chicken/Victoria/1/92	H7N3	18 000	One chicken farm, duck farm with H7 antibodies
12 A/chicken/Queensland/667-6/94	H7N3	22 000	One farm
13 A/chicken/Mexico/8623-607/94	H5N2	Unknown – millions?	Many farms
14 A/chicken/Pakistan/447/94	H7N3	>6 000 000	Many farms
15 A/chicken/NSW/97	H7N4	310 000	Two chicken, one emu farms
16 A/chicken/Hong Kong/97 [†]	H5N1	3 000 000	All poultry in Hong Kong slaughtered
17 A/chicken/Italy/330/97	H5N2	8000	Eight farms
18 A/turkey/Italy/99	H7N1	14 000 000	413 farms
19 A/chicken/Chile/2002	H7N3	c. 700 000	Two farms
20 A/chicken/Netherlands/2003	H7N7	c. 30 000 000	241 in the Netherlands; eight in Belgium; one in Germany
21 A/chicken/Eurasia and Africa [‡] /2003-6	H5N1	Unknown – hundreds of millions	Hundreds/thousands ongoing
22 A/chicken/Texas/2004	H5N2	6600	One farm
23 A/chicken/Canada-BC/2004	H7N3	17 000 000	42 commercial, 11 backyard – all poultry in Fraser Valley area culled
24 A/ostrich/South Africa/2004	H5N2	30 000	Many, ongoing

*Where outbreaks were extensive and infecting different types of poultry the first reported virus is listed.

[†]Probably early outbreak of 21.

[‡]Nineteen Asian, seven European and five African countries had reported outbreaks in May 2006.

more than 500 000 dying or being slaughtered, eight of the second 12 greatly exceeded 500 000 birds (Table 1).

The reasons for the apparent increase in both numbers of outbreaks and their impact are likely to be extremely complex and a product of a number of factors: greater awareness and diagnostic capabilities; changes in poultry production such as establishing densely populated poultry production areas, integrated production systems and a move towards rearing birds on open range; more open reporting and investigation of disease; and possibly changes in wild bird movements as a result of climatic change, have all been suggested as potentially contributing.

Effect of vaccination on the epidemiology of AI

For many years, vaccination against HPAI viruses and therefore LPAI of H5 or H7 subtypes was actively discouraged or banned in some countries because it was consid-

ered that it would interfere with the diagnosis of HPAI. Vaccination with autogenous inactivated vaccines was carried out in a few areas where LPAI viruses of other subtypes were a problem, mainly in turkeys, in the USA and Italy. However, the marked increase in outbreaks of HPAI since the 1990s and the spread of H9N2 infections across Asia have led to considerable pressure to use vaccination as part of control policies, either as an emergency measure or prophylactically for both HPAI and LPAI. Optimal vaccination with currently available AI vaccines when selected properly and administered correctly will protect against clinical signs and mortality, reduce the levels and duration of virus excretion and increase the resistance of the host to infection by raising the minimum infectious virus dose needed to infect the bird.⁶³ However, AI viruses (especially HPAI) may still infect and replicate in vaccinated birds without the presentation of clinical signs, although the virus may ultimately die out in an infected vaccinated flock.⁶⁴

There is no doubt that when used properly, usually in addition to, rather than instead of, other measures such as increased biosecurity and stamping out vaccines may be a powerful tool in the eradication of AI infections.⁶⁵ However, it is possible that suboptimal vaccination may result in the reduction of disease without affecting transmission, resulting in an endemic situation⁶⁶ and the potential for antigenic drift and variation in the endemic virus.⁶⁷ For this reason, vaccination should only be part of a wider control strategy, which must include improved biosecurity and the detection of field-exposed flocks within the vaccinated population.⁶⁸

Discussion

The epidemiology of AI has changed in the last 10 years, not only because of the failure to control and eradicate infections in poultry due to LPAI H9N2 viruses and Asian HPAI H5N1 viruses, but also because the continued development and industrialization of the poultry industries throughout the world have meant that AI infections, especially HPAI outbreaks, have had a far greater impact in terms of spread and loss of birds than in the earlier years. In addition, in the past, the spread of HPAI virus to wild birds has not been recorded on the scale reached by the Asian HPAI H5N1 virus. Whether the virus is likely to become or remain endemic in some species of wild birds or would gradually die out if there was no further spread from infected poultry is not clear.

This change in the ecology and epidemiology of AI infections requires the urgent generation of new knowledge on issues related to epidemiology, pathogenesis and control. The Asian HPAI H5N1 viruses have spread to three continents, with completely different agricultural, ecological, social and economic backgrounds. This, in turn, is likely to result in the establishment of different mechanisms by which the virus may be perpetuated in a given area. The generation of such cycles will be influenced by the diversity and availability of hosts in that area. As the virus encounters new hosts – within and outside the class *Aves*, it may well acquire mutations that may reflect replication advantages in one or more species, but affect the pathogenicity and transmissibility in those and other species.

In view of the zoonotic potential, it would appear important that the Asian HPAI H5N1 virus (and probably the H9N2 virus) is eliminated from poultry and not just contained by the use of vaccination, as has been the strategy with other poultry viruses, especially Newcastle disease virus,⁶⁹ which remains endemic in many parts of the world. Additionally, the application of control programmes encompassing vaccination may result in the generation of strains that have progressively drifted away from the original antigenic profile.⁶⁷ To date, it is unclear how the

immunological pressure generated by the variety of seed strains contained in the available and planned veterinary vaccines will affect the antigenic properties of isolates.

The results of these two driving forces in the genetic and antigenic profile require careful monitoring of viral strains and a close collaboration between the parties involved in the crisis management. The monitoring effort should aim at the collection and characterization of strains to identify genetic mutations and antigenic properties. Information should be collated and made available to the international scientific community, so that those involved in both animal and human health are fully informed of the current situation.

Efforts to bring about control and eradication internationally will have to take into account the extremely complex situation, especially in any given geographical location, the characteristics of the poultry-producing sector in its entirety, the eco-epidemiological situation, the response capacity of the veterinary infrastructure and the availability of adequate resources. These features must be integrated with the social environment, including those linked to the rearing of birds for recreational and farming purposes. It is possible that in some areas control and eradication will never be achieved and great changes in the way poultry are reared and they and their products marketed will be necessary.

For this reason, international organizations that govern trade regulations and animal disease control should establish a set of guidelines so that control programmes may be 'accredited' and consequently internationally recognized. Such a policy would appear to have several practical advantages, ultimately resulting in an improved crisis management. These include rapid approval of established control programmes, constant update on the field situation, feedback of information on successes and failures, harmonization of protocols and systems and public availability of control and eradication programmes. In this way, even inexperienced countries can maximize the outcome of other experiences to combat this infection in an educated manner – thus avoiding wastage of resources and time.

At least two AI subtypes, H5N1 and H9N2, both of which have zoonotic implications are currently endemic in vast areas of the world. It is impossible to predict whether either of them will represent the progenitor of the next human pandemic virus. Certainly, both of them are causing losses to the poultry industry and H5N1 is also causing the loss of human lives and the reduction in the livelihood of rural establishments. The extensive and uncontrolled circulation of these strains could result in catastrophic consequences for both human and animal health and therefore requires an extraordinary and coordinated international effort so that control and eradication can be successfully managed and achieved.

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