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Strategic challenges in the global control of high pathogenicity avian influenza

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Summary

H5Nx A/Goose/Guangdong/1/96 Eurasian lineage high pathogenicity avian influenza (HPAI) viruses have been the main HPAI strains detected globally since 2005. These have spread around the world, causing a panzootic that has spanned six continents, with continual threat to not only wild and captive birds and poultry, but also wild, captive and domestic mammals and humans. The viruses' ecology and epidemiology – especially the 2.3.4.4b clade – have changed, with over 489 species of birds infected and spreading the virus over migratory routes. This results in the death of many birds, including endangered species, and serves as a source of transmission to poultry and mammals. Improved surveillance and sharing of HPAI virus sequences, metadata and viruses across the veterinary, public health, wildlife and environment sectors are needed to elucidate the population dynamics of the infections, which is crucial to addressing this complex One Health issue. The development of appropriate mitigation strategies or changes in husbandry, production and selling practices can reduce the risk of viruses being introduced into farms, as well as their amplification and viral evolution, and any spill-back to wild birds. Approaches to prevention and control of HPAI in countries where these 2.3.4.4b viruses remain entrenched in poultry, or places at risk of virus introduction via wild bird populations, involve measures to reduce the effects of the disease in poultry (including enhanced farm biosecurity, vaccination, zoning and compartmentalisation). Their uptake reflects the difficulties encountered in relying solely on biosecurity for disease prevention and on stamping out alone for virus control and elimination. The World Organisation for Animal Health's *Terrestrial Animal Health Code* allows use of vaccination of poultry under specific conditions and without negatively impacting HPAI-free status if appropriate surveillance is conducted, thus supporting safe trade in poultry and poultry products. Nevertheless, concerns regarding loss of valuable export markets still interfere with greater utilisation of vaccination.

Keywords

Avian influenza – Compartmentalisation – Control – H5N1 – High pathogenicity – One Health – Prevention – Vaccination – Vaccines – Zoning.

Introduction

Avian influenza (AI) viruses are classified, based on surface glycoproteins, into 16 hemagglutinin (H1-16) and 9 neuraminidase (N1-9) subtypes [1]. In addition, AI viruses are categorised into two pathotypes, low pathogenicity AI (LPAI) and high pathogenicity AI (HPAI), based on *in vivo* tests in chickens (intravenous pathogenicity index greater than 1.2) or detection of the genetic correlates for pathogenicity at the proteolytic cleavage site of the hemagglutinin [1,2]. To date, all H1-H4, H6 and H8-H16 viruses have been LPAI, while H5 and H7 can be either LPAI or HPAI, with HPAI viruses arising by mutation of the gene segment coding for hemagglutinin of LPAI viruses, usually following replication in chicken or turkey hosts. An infection with HPAI virus in poultry, wild birds and non-poultry domestic birds is notifiable to the World Organisation for Animal Health (WOAH) [3]. LPAI viruses that have proven natural transmission to humans with severe consequences or those causing an unexpected increase in virulence in poultry are also reportable to WOAH. In addition, LPAI viruses in wild birds can be reported on a voluntary basis, through the voluntary report on non-WOAH-listed diseases in wildlife [1,4]. Furthermore, WOAH Members are instructed not to impose bans on international trade of poultry commodities when notified of HPAI in only wild birds or non-poultry.

Since 1959, 50 distinct H5 and H7 hemagglutinin HPAI virus lineages have been identified [5-7]. Between 2005 and 30 August 2023, H5 and H7 HPAI were notified to WOAH by 122 Members and non-Members across the WOAH regions of Africa, Asia and the Pacific, the Americas, Europe and the Middle East (Figs 1–3). A total of 40,372 outbreaks were reported (in poultry,[1] non-poultry domestic birds and wild birds), resulting in over 31 million reported domestic and wild bird deaths and 451 million domestic birds culled. The main strains reported were H5Nx viruses of the A/Goose/Guangdong/1/96 (Gs/GD) Eurasian lineage, which emerged and have circulated as HPAI viruses since 1996.

Wild aquatic birds serve as the genetic reservoirs of all LPAI viruses, with occasional transfer of these viruses to poultry and resulting adaptation and onward spread within poultry populations [8]. However, for certain LPAI virus lineages, poultry must be considered the main reservoir (e.g. H9N2 Eurasian lineage viruses in much of Asia, the Middle East and some African countries). Historically, wild aquatic birds have not had significant involvement in the epidemiology of HPAI, but this changed with the emergence of the H5Nx Gs/GD Eurasian lineage. The H5Nx Gs/GD virus has genetically diversified through mutations to form multiple hemagglutinin genetic clades and subclades. Furthermore, Gs/GD viruses have been highly active in reassortment processes with various LPAI viruses. This has led to the emergence of hundreds of different genotypes, each with unique biological features, including, for some genotypes at least, increased fitness for a particular domestic or wild bird host species or ecosystem.

In 2020, H5N8 clade 2.3.4.4b viruses re-emerged after initial incursions in 2016 and spread from central Asia to Europe, eastern Asia, the Middle East and Africa (Fig. 4). After reassorting in Europe and crossing the north Atlantic, the H5N1 2.3.4.4b virus was detected in Newfoundland, followed by extensive outbreaks during winter and spring 2022 in Canada and the United States of America (US). In late 2022, the virus moved into Mexico and Central and northern South America, and in winter and spring 2023 down the Pacific coast, inland and up the Atlantic coast of South America. In late 2023, the virus was detected in wild birds in sub-Antarctic South Georgia and in February 2024 in Antarctica. In multiple geographic locations, the virus has caused extensive infections in diverse species of wild and captive aquatic and non-aquatic birds, and in poultry and other domestic birds, with spillover infections in wild mammals, farmed mink and foxes, dairy cattle and other livestock, and occasionally domestic cats and dogs and mammals in zoological collections, as well as sporadic human infections.

Challenges to high pathogenicity avian influenza control in the diverse poultry industries

The HPAI virus is generally highly transmissible, causing severe disease with high mortality in unvaccinated galliform poultry (chickens, turkey, quail, etc.), irrespective of the production system [1,4], but Gs/GD viruses can also cause subclinical infection in domestic ducks. Flocks of infected domestic ducks may have low to no mortality but serve as a local reservoir for virus replication, shedding, environmental contamination and spread to galliform poultry and potential re-exposure and infection of wild birds. Understanding poultry value chains is essential to support the development of effective prevention and control strategies. The design and implementation of a farm or premise biosecurity plan tailored to the different risk pathways is the principal mitigation strategy to prevent the introduction of the HPAI virus among a naive population from affected domestic birds or, in relation to the H5Nx Gs/GD Eurasian HPAI viruses, by wild bird carriers and their contamination of surrounding environments.

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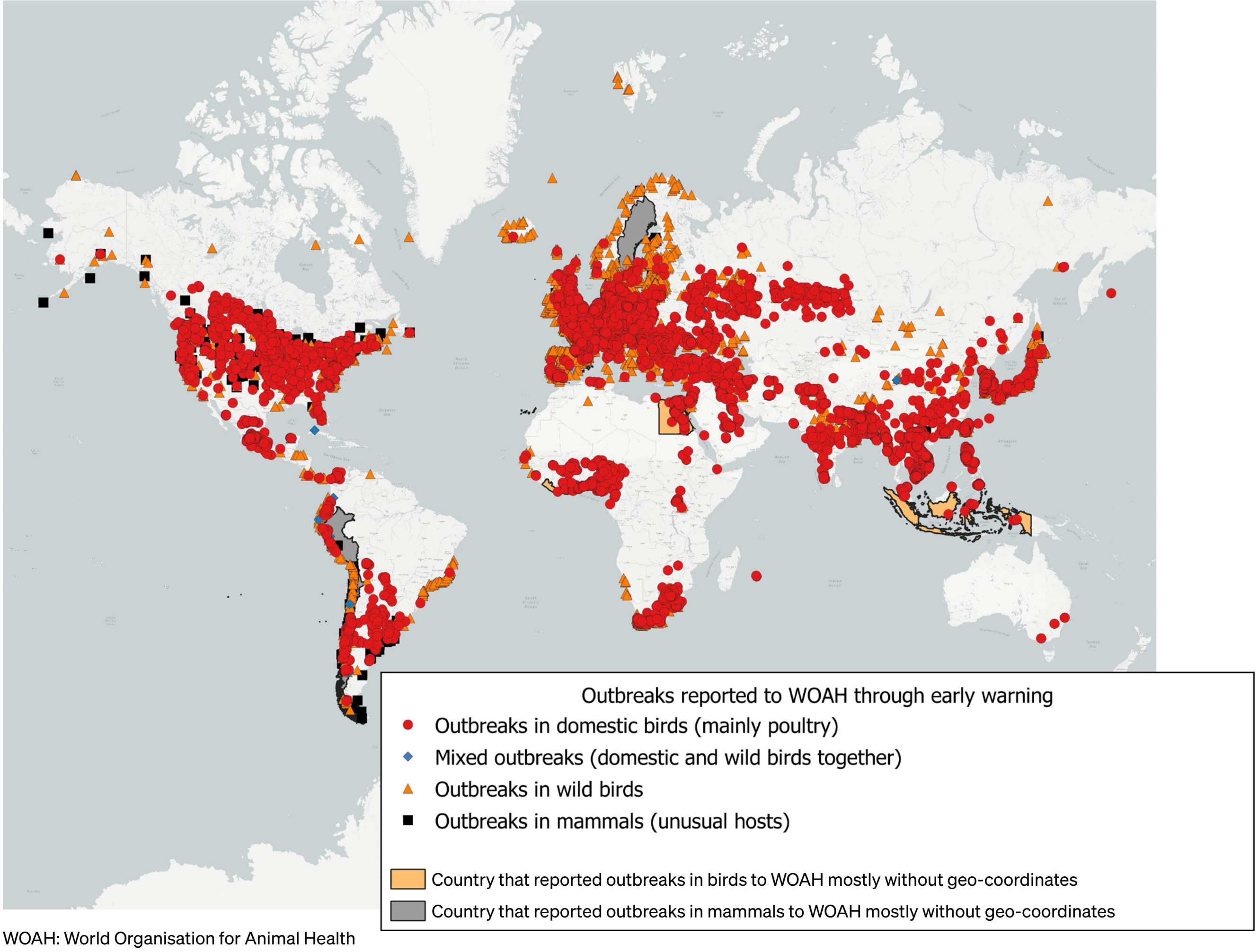
[1] For the purpose of the *Terrestrial Animal Health Code* (2022), ‘poultry’ refers to all birds reared or kept in captivity for the production of any commercial animal products or for breeding for this purpose, fighting cocks used for any purpose, and all birds used for restocking supplies of game or for breeding for this purpose, until they are released from captivity. Birds that are kept in a single household, the product of which are used within the same household exclusively, are not considered poultry, provided that they have no direct or indirect contact with poultry or poultry facilities. Birds that are kept in captivity for other reasons, including those that are kept for shows, racing, exhibitions, zoological collections and competitions, and for breeding or selling for these purposes, as well as pet birds, are not considered poultry, provided that they have no direct or indirect contact with poultry or poultry facilities.



WOAH: World Organisation for Animal Health

Figure 1

Cumulative reported presence of H5 and H7 high pathogenicity avian influenza from 2005 to 2023 (as of 30 August 2023)

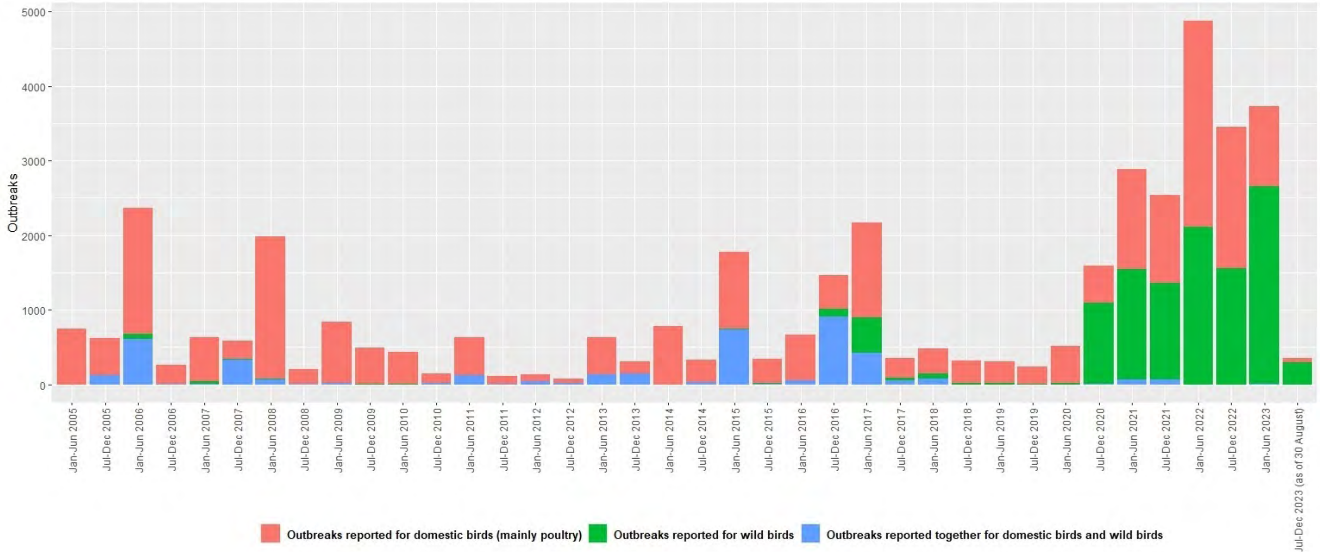


Figure 2

Number of H5 and H7 high pathogenicity avian influenza outbreaks reported by animal category (as of 30 August 2023)

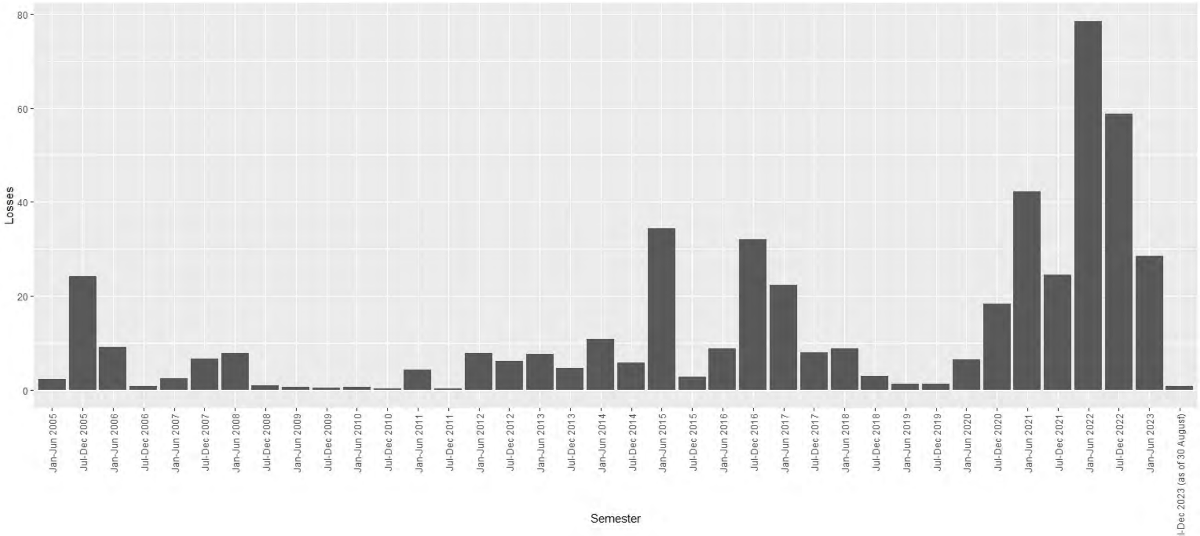


Figure 3

Number of deaths (millions), including by culling, of domestic birds affected by H5 and H7 high pathogenicity avian influenza from 2005 to 2023 (as of 30 August 2023)

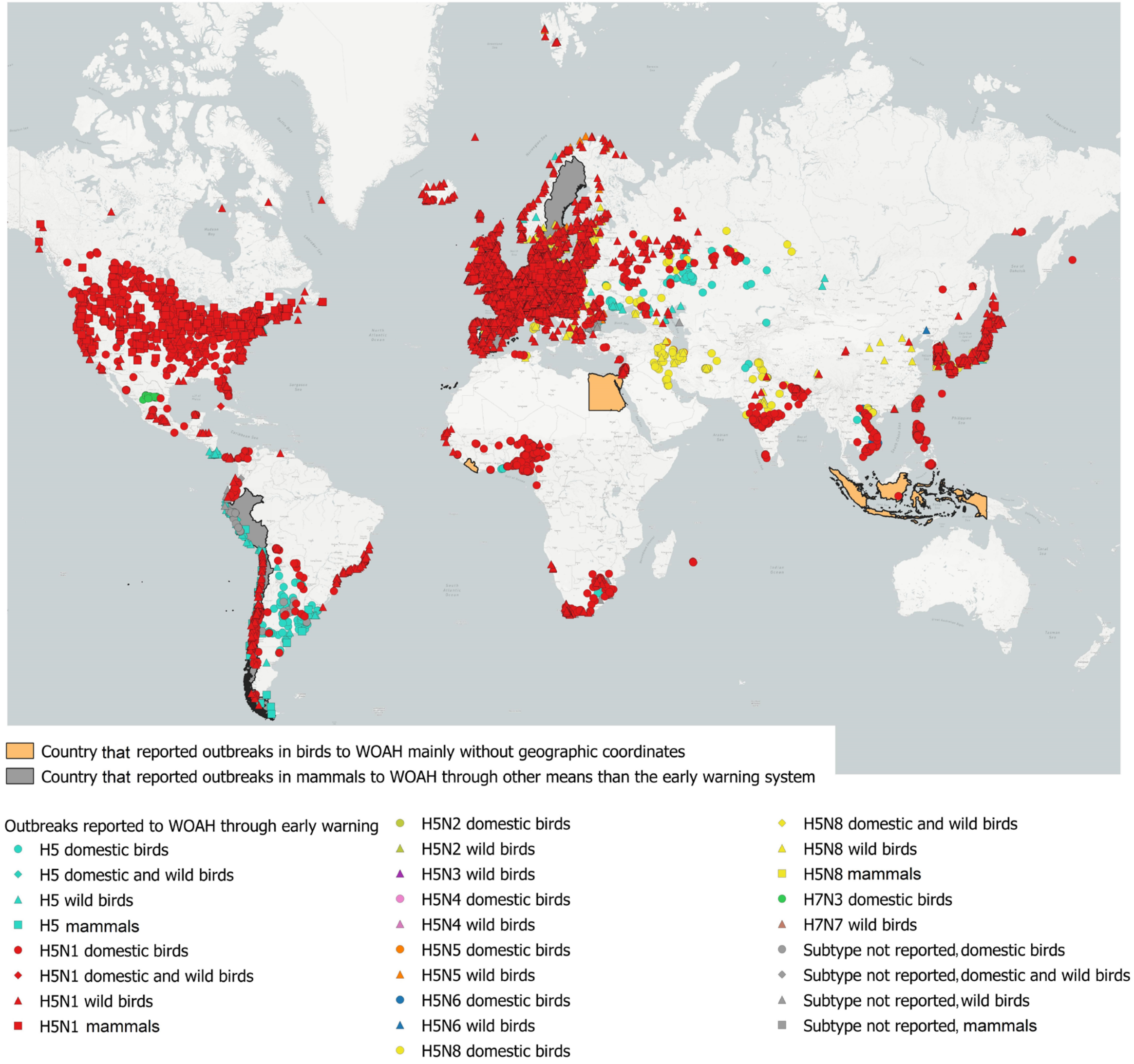


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Figure 4

Geographic spread of the 2.3.4.4b A/Goose/Guangdong/1/96 high pathogenicity avian influenza virus predominantly from October 2020 through August 2023

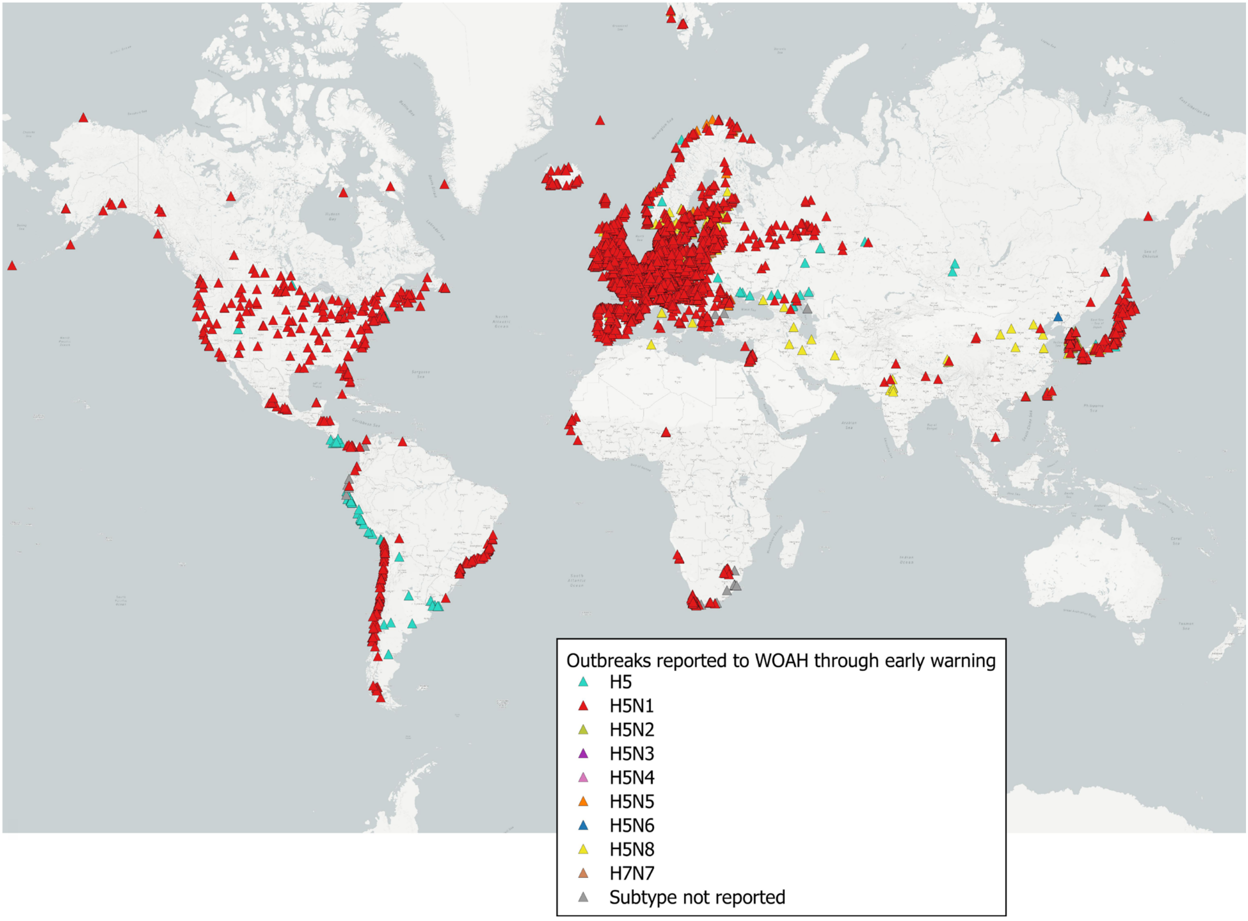
Since 1996, the Gs/GD Eurasian lineage has produced multiple intercontinental waves of transmission via wild birds, the largest caused by clade 2.3.4.4b viruses, reported in over 489 wild, captive and domestic bird species, with varying outcomes ranging from asymptomatic infections to individual bird mortality to massive die-offs in breeding colonies of specific bird species, thus negatively impacting avian biodiversity [9]. The current panzootic has demonstrated that, for certain production systems (e.g. turkey, chicken layer and foie gras production), biosecurity measures alone do not prevent all incursions of clade 2.3.4.4b viruses, and other methods to prevent transmission in flocks are warranted, including vaccination.

Key changes driving the 2.3.4.4b A/Goose/Guangdong/1/96 Eurasian lineage high pathogenicity avian influenza panzootic

Ecological and epidemiological changes in wild birds and mammals

It became apparent that wild birds could transmit Gs/GD HPAI viruses over long distances when cases of HPAI occurred in Japan and the Republic of Korea in 2003–2004 [10-12]. Subsequent transregional and/or transcontinental spread of Gs/GD HPAI by wild birds occurred during five time periods (2005–2008 [clade 2.2], 2009–2010 [clade 2.3.2.1], 2014–2015 [clades 2.3.4.4 and 2.3.2.1c], 2016–2017 and 2020–2023 [both involving clade 2.3.4.4b]) [13]. Prior to the 2020 re-emergence of clade 2.3.4.4b viruses, infection in wild birds did not persist.

The most recent series of wild bird HPAI cases (clade 2.3.4.4b, October 2020–August 2023) has had the widest geographic spread, with 101,817 wild bird cases (many associated with mass mortality events) in over 76 countries and territories across Africa, the Americas, Antarctica, Asia, Europe and the Middle East (Fig. 5), a historically unprecedented occurrence. This virus clade is highly infectious for domestic and wild ducks, requiring only small infectious virus doses, with subsequent virus shedding exceeding 14 days [14,15]. As a result of this ecological change, the 2.3.4.4b clade is broadly adapted to birds and has become established in some wild aquatic bird populations, with spillover into scavenger and predatory birds and wild mammals [16]. Thus, infected migratory aquatic birds serve as a vector of this virus, triggering transmission to



WOAH: World Organisation for Animal Health

Figure 5

Reported outbreaks of high pathogenicity avian influenza in wild birds between October 2020 and August 2023

outdoor-reared domestic birds or indirectly disseminating the virus through breaches in biosecurity from contaminated environments outside of poultry barns. Wild aquatic birds have introduced the HPAI virus to indigenous populations of wild bird species with independent maintenance and contribution to further virus diversity. Furthermore, mass mortality events have been reported for many wild aquatic and non-aquatic birds species, such as common cranes (*Grus grus*) in Israel [17], African penguins (*Spheniscus demersus*) and Cape cormorants (*Phalacrocorax capensis*) in southern Africa [18], Peruvian pelicans (*Pelecanus thagus*) and brown boobies (*Sula leucogaster*) in South America [19], Sandwich terns (*Thalasseus sandvicensis*) in the Netherlands [20], great skuas (*Stercorarius skua*) and northern gannets (*Morus bassanus*) in Great Britain [21], turkey vultures (*Cathartes aura*) and black vultures (*Coragyps atratus*) in the US [22] and brown skuas (*Stercorarius antarcticus*) on South Georgia Island [23]. Such large mortality events have had a negative impact on wild bird populations, changing the diversity of species in critical ecosystems and further endangering threatened avian species.

Increasing numbers of clade 2.3.4.4b virus infections are being reported in wild and captive mammals, including 37 species of terrestrial carnivores scavenging infected wild birds, such as red foxes (*Vulpes vulpes*), skunks (*Mephitis mephitis*), common raccoons (*Procyon lotor*), mountain lions (*Puma concolor*) and various bears, and in 12 species of sea mammals, including 164 harbour seals (*Phoca vitulina*) and over 10,000 sea lions (*Otaria flavescens*) within Europe and the Americas [9,24,25]. Outbreaks of clade 2.3.4.4b occurred in farmed mink in Spain in October 2022 [26], and in foxes, minks and raccoon dogs on 25 farms in Finland in July 2023 [27]. Furthermore, clustered cases in domestic cats in Poland and the Republic of South Korea in 2023 raised additional concerns for potential transmission to humans. The continued introduction and circulation of these viruses in mammals provide opportunities for stepwise adaptation to mammals through mutations and selection, and for potential reassortment of gene segments, which could increase their pandemic potential for humans.

Epidemiological changes in poultry and other domestic birds

Originally, classical HPAI developed from H5 or H7 LPAI virus after direct or indirect exposure of poultry to infected wild birds, followed by mutation in galliform poultry to an HPAI virus and circulation in poultry, with premises-to-premises spread of the virus on fomites through human activity and possibly some contribution by aerosols [28,29]. Typically, the farm gate has been the point of control, and the process uniformly used was stamping out through a combination of diagnostics and surveillance to locate the virus, quarantine of affected premises, movement controls on poultry within the infected zone, culling of poultry on affected premises, and cleaning and disinfection to destroy the virus in the affected barns. Historically, migratory aquatic birds have not been involved in the epidemiology of HPAI epizootics. Of the 50 unique HPAI events since 1959, 42 were eliminated, usually within a few weeks to several years, using a stamping-out programme. As an example, in 2015, an H7N7 LPAI virus mutated to HPAI, affecting chicken layers on two farms in Germany, with elimination accomplished in a few weeks by stamping out [30].

The change in the epidemiology of HPAI in poultry occurred with the H5Nx Gs/GD Eurasian lineage as a result of the continued exposure to, infection of and transmission to domestic waterfowl, many of which were asymptomatically infected, as well as the expansion with infection and spread by migratory waterfowl species beginning in 2002 [10]. In 2014, clade 2.3.4.4c was introduced into North America by migrating waterfowl crossing the Bering Strait from Asia [31]. The first cases were due to transmission from wild birds to captive hunting raptors and to backyard galliform and anseriform domestic birds [31,32]. Initially, this virus was highly adapted and transmissible to mallard and domestic ducks but poorly adapted to chickens and turkeys, requiring high infectious doses, and was poorly transmissible [33-35]. The initial commercial poultry cases were in California, Arkansas, Missouri and Minnesota during winter 2015 and were point source introductions by indirect contact with wild waterfowl [31,32]. However, from March to June, most of the poultry cases resulted from farm-to-farm spread without wild bird involvement [32].

In 2014–2015, the 2.3.4.4c virus infection pressure and environmental contamination by wild aquatic birds was low, with only 98 confirmed wild bird cases across 20 species in 15 US states and 211 commercial and 21 backyard poultry premises in 21 states affected [36,37]. Afterwards, wild bird detections declined in the US, with two detections in the 2015–2016 season, one in the 2016–2017 season, none in subsequent surveillance seasons up to 2020–2021, and no Gs/GD Eurasian lineage cases on commercial or backyard premises [38]. However, in 2021, clade 2.3.4.4b entered North America via the North Atlantic from Europe, resulting in over 7,355 virus detections in over 155 wild bird species in 49 US states and more than 206 cases in wild mammals in 18 species in 26 US states (31 December 2021 to 6 November 2023) [39]. This higher wild bird infection rate compared to the 2014–2015 outbreak and broader geographic footprint were associated with a higher infection rate in backyard birds (515 cases) and a lower infection rate in commercial poultry (325 cases) [39]. Genomic analysis supported that 85% of backyard and commercial farm cases resulted from point source introductions and only 15% from potential onward spread from farm to farm [40]. Similarly, Europe had a large proportion of cases in domestic poultry through point source introductions. In some sectors, particularly domestic ducks, farm-to-farm spread occurred.

Because of the spread of the Gs/GD lineage of viruses by migratory birds, the biosecurity barrier has now moved from the farm gate to the barn door as the 'line of separation' between the contaminated environment around the barn (curtilage) and the poultry inside. Stamping out has been effective in eliminating the virus from affected farms, thus reducing or eliminating farm-to-farm transmission, but introductions from wild birds create an ongoing threat. This challenges the socio-economics of stamping-out programmes as the principal outbreak management tool. Consumer concerns and political resistance to a blank check for stamping out have increased, while compensation and indemnification costs have been deemed unsustainable. The ongoing outbreaks have had a negative impact on commercial production as well as rural livelihoods and farmers' mental health. In addition, consumers have seen the cost of goods increase; for example, in the US and the European Union, egg prices increased by 155% and 62%, respectively, in the first quarter of 2022 [41]. The welfare of birds is a concern not only in terms of death and suffering, but also because of the depopulation of large numbers of seemingly healthy poultry (over 58 million in the US alone), loss of high-quality protein from this food supply and lack of free-range outdoor production.

Zoonotic features

Before 1996, human cases of AI viruses were exceedingly rare, but with the appearance of the H5Nx Gs/GD Eurasian lineage, human infections have increased, raising the potential for emergence of the next human pandemic viruses from an AI virus. Sporadic human infections have been caused by the H5Nx Gs/GD lineage HPAI (H5N1 since 2003: 878 cases, 458 fatalities; H5N6 since 2014: 87 cases, 33 fatalities) and, since 2013, the H7N9 Eurasian lineage LPAI and HPAI viruses (1,568 cases, 616 fatalities) [25]. Some molecular markers, indicative of adaptation to mammals, including humans, have been reported for H5Nx Gs/GD viruses, but neither H5 nor H7 HPAI virus lineage has exhibited sustained human-to-human transmission. Human infection with AI is reportable to the World Health Organization under the International Health Regulations (2005) [42].

Global control strategies

Country-based high pathogenicity avian influenza eradication programmes

The WOAH General Session of May 1964 included HPAI (i.e. fowl plague) for compulsory notification either monthly or every two weeks to facilitate Members' efforts to prevent the introduction of the disease via international trade in birds and their products. Since 1959, scientific and technological advances have improved the speed of the stamping-out process in well-resourced countries, thus shortening the time between suspicion, confirmation and elimination of HPAI. These advances include development and implementation of:

- a single incident command system with real-time electronic communication to facilitate unified and coordinated response on national and state/provincial levels with all involved entities;
- data collection and analysis capacity that support HPAI management and response decisions;
- strong public–private partnerships between national and state governments and private sector companies to develop trust, cooperation and coordinated response activities;
- compensation and indemnification mechanisms to maintain the livelihoods of farmers, in turn encouraging early reporting of suspicious HPAI cases;
- rapid molecular diagnostics and surveillance assays, coupled with commercial couriers to rapidly move samples from field to diagnostic laboratories, which together have shortened the time from suspicion to confirmation of HPAI;
- novel methods to facilitate mass depopulation, with a 24-hour goal for completion on a single farm [43];
- environmentally sound methods for disposal of carcasses, such as composting and rendering; and
- new methods for wet and dry virus elimination within barns and environments and on equipment.

These advancements have been incorporated into the stamping-out programmes of many countries, improving the success of elimination. However, the H5Nx Gs/GD lineage has shown that elimination by stamping-out programmes alone is costly and not sustainable because of continual pressure of reintroduction from wild birds. In most low-to middle-income countries, the nature of the poultry production and selling systems, capacity issues with Veterinary Services, weak signals of infection in domestic ducks, and limited incentives to report disease, including the lack of compensation, mean that stamping out is not sufficient to eliminate the virus. Most low- to middle-income countries in Asia and Africa have not been able to eliminate the virus once it is entrenched in poultry. Zoning (regionalisation) and compartmentalisation have eased country-wide geographic restrictions to smaller risk areas or low-risk premises in some countries, allowing continued safe supply and even export of poultry and poultry products.

Country-based high pathogenicity avian influenza vaccination programmes reported through the World Animal Health Information System

Vaccination has been used in a limited number of countries as an emergency or systematic measure to protect poultry or other captive bird populations from H5 and H7 HPAI, especially when the disease cannot be rapidly contained by methods based on stamping out, or when existing biosecurity measures along the value chain are insufficient alone to prevent HPAI [4]. In 1995, both Mexico and Pakistan faced entrenched HPAI viruses and implemented vaccination as a complementary tool alongside enhanced biosecurity and stamping-out programmes, with Mexico achieving elimination by the end of 1995 and Pakistan reporting its last H7N3 HPAI case in 2004 [44]. Beginning in 1996, the Gs/GD viruses emerged in the People's Republic of China (PR China), and over the next five years they became entrenched and evolved into multiple clades and genotypes. From 2003, Gs/GD viruses extended to other east and southeast Asian countries [45]. Hong Kong, Special Administrative Region of PR China, implemented emergency and then systemic vaccination from 2002 because existing biosecurity measures in farms and markets were insufficient. Once Gs/GD virus was entrenched or enzootic in poultry populations, vaccination was implemented to assist in disease prevention to maintain food security and rural livelihoods in PR China, Indonesia, Egypt, Vietnam and Bangladesh [44,46,47]. In Vietnam, vaccination was introduced in 2005 after some 30 million poultry had been destroyed but the virus was not eliminated and human cases were still occurring [10]. Vaccination likely reduced zoonotic spillover.

In the mid-2000s, a few countries used emergency vaccination (Côte d'Ivoire, Sudan, Democratic People's Republic of Korea, Israel, Russia and Pakistan) and were able, in combination with stamping out in poultry, to eradicate the virus from their countries. In addition, preventive systematic to targeted vaccination was used in a few (Mongolia, France and the Netherlands) to many (Kazakhstan) commercial flocks to protect poultry at high risk of HPAI [44,48]. Systematic vaccination of poultry has also been used successfully in PR China since 2017 to reduce the zoonotic threat posed by H7N9 HPAI viruses. In addition, successful HPAI vaccination programmes were undertaken in 13 European Union countries in zoo birds (non-poultry) in the mid-2000s [49]. Official and unofficial vaccination of poultry occurs in additional countries in Asia and Africa. Since the incursion of Gs/GD HPAI viruses into the Americas, emergency vaccination has been implemented in Mexico, Guatemala, Ecuador, Peru, Bolivia and Uruguay. Other countries are considering vaccination, and trials have been conducted in France, Italy and the Netherlands as an initial step towards introduction of preventive vaccination. France commenced vaccination of ducks in October 2023.

Emerging strategic national challenges in the global control of high pathogenicity avian influenza

WOAH provides science-based guidelines for the prevention, control and elimination of HPAI through the *Terrestrial Animal Health Code* (*Terrestrial Code*) and the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*), as well as other publications and conferences based on the collective inputs of WOAH AI Reference Laboratories, several WOAH Collaborating Centres and AI experts in the WOAH/Food and Agriculture Organization of the United Nations Network of Expertise on Animal Influenza (OFFLU; https://www.offlu.org). These have helped develop national control and eradication strategies. However, the changing ecology and epidemiology of HPAI (especially clade 2.3.4.4b but also other clades) and its negative socioeconomic impact have challenged the old paradigm of eradication through nationally driven stamping-out strategies alone.

Avian influenza intelligence strategies: surveillance and monitoring for early detection and prevention

Detection of HPAI virus (mostly 2.3.4.4b) in a wide range of migratory, scavenging, predatory and resident birds across six continents from October 2020 through August 2023 highlights a continuing threat. Infection persists in wild bird populations, creating a highly mobile reservoir spreading the virus over vast distances and contaminating the environment. This has led to significant infection and mortality and the decline of breeding colonies of various endangered or threatened bird species, particularly seabirds. This, in turn, has led to multiple HPAI virus incursions to animal agriculture and some spill-back from infected poultry into wild birds. This changing ecological and epidemiological situation has led to infections and deaths in terrestrial and sea mammals, and to sporadic human infections. To better comprehend and mitigate the changing ecology of 2.3.4.4b HPAI and its effects on domestic birds and wildlife, nations must strengthen their monitoring and surveillance of wild bird populations, to close crucial knowledge gaps concerning affected species, and combine this knowledge with domestic bird surveillance to create an effective HPAI early warning system. Cooperative regional programmes should be developed to share sequences, viruses and knowledge, especially along wild aquatic bird migratory flyways. Investment in genotype–phenotype understanding of virus biology in poultry and wild birds will further assist in understanding risks and their mitigations. Poultry production processes should be assessed to improve farm biosecurity and reduce risks of introduction and spill-back.

Vaccination as a supplemental disease control strategy for business continuity

Poultry vaccination can be used to prevent AI infections in at-risk regions and to assist stamping-out programmes in maintaining poultry production and livelihoods in entrenched areas when eradication is not immediately feasible. Use of high-potency vaccines with appropriate antigenic match to field viruses can provide protection from illness and death and increase resistance to HPAI, such that a 1,000–10,000 times greater virus exposure dose is required to produce infection and, if infections occur, the birds excrete 100–100,000 times less virus, thus greatly reducing poultry infections and subsequent environmental contamination. This translates into reduced transmission, as quantified by a reproduction ratio (R) below 1 [50,51]. As a result, onward transmission is prevented, and environmental contamination by HPAI virus and exposure of humans and other mammals is minimised and even prevented. If R is reduced, although not to R<1, vaccination still may have benefits in reducing clinical disease and production losses. If R is close to 1, outbreaks will be reduced in number and size, environmental contamination will decrease, and the probability of onward spread to other farms will be lower if adequate biosecurity and surveillance are in place. A further benefit will be a reduction in additional virus evolution and potential consequential changes in risk profile [52]. From a technical perspective, appropriate surveillance systems can be designed and implemented for vaccinated poultry to demonstrate freedom from infection, and if infection should be detected in vaccinated flocks, those flocks would still be subject to a stamping-out strategy. However, despite the global threat and scientific support for vaccine usage, vaccination is not extensively used as a disease control measure by countries exporting poultry and poultry products, mostly due to the potential negative impact on international trade.

Vaccination can be effective, as a complementary tool, for the prevention, management or elimination of HPAI depending on the individual countries' HPAI status and available resources. Effective strategies should contain:

- a risk-based, logistically feasible, cost-effective, targeted vaccination programme designed for specific poultry populations and geographic areas within individual countries;
- co-development of vaccination programmes through public–private partnerships;
- availability of registered vaccines and understanding of how they would fit into a vaccination programme;
- modification of the regulatory process to accelerate antigenic updating of seed strains or hemagglutinin gene inserts; and
- science-based programmes to monitor vaccinated populations for protective immune response and detection of any potential HPAI virus circulation.

Vaccination will not affect the HPAI status of a free country or zone if surveillance supports the absence of infection [4]. OFFLU has developed the Avian Influenza Matching report (https://www.offlu.org/wp-content/uploads/2023/11/OFFLU-AIM-REPORT-2023.pdf) to scientifically assess the genetic and antigenic relatedness of HPAI viruses. This programme can assist countries in matching the hemagglutinin of inactivated vaccines to field viruses in order to provide and maintain optimal protection.

International standards to facilitate safe trade, including in the presence of vaccination

The *Terrestrial Code* provides outcome- and risk-based solutions to protect animal health and welfare during production and allow safe trade in animals and animal products while avoiding unjustified sanitary barriers to trade [4]. The *Terrestrial Code* supports the prevention and control of HPAI by:

- promoting HPAI-free areas at the country, zone or compartment level based on appropriate supporting surveillance programmes;
- accepting the use of vaccination under specific conditions;
- acceptance of an HPAI outbreak containment zone within a country or zone free from HPAI;
- promoting a scientifically based process for recovery of the HPAI-free status of a country or zone after an incursion;
- recommending science-based provisions for the safe importation of various poultry commodities, according to the animal health status of the population and any mitigations utilised; and
- listing safe commodities for import or transit irrespective of HPAI status of the exporting country or zone.

National regulations should be harmonised with WOAH International Standards to allow trade when appropriate vaccination, zoning and compartmentalisation are utilised in HPAI control programmes. This can be facilitated by development of surveillance programmes to demonstrate the safety of poultry and poultry products from vaccinated flocks and HPAI-free zones and compartments. Guidelines for diagnostic techniques and vaccines for HPAI are covered in the WOAH *Terrestrial Manual* [1]. Unfortunately, not all countries are prepared to accept poultry from countries where vaccination is used, and this inhibits vaccination in places where it would likely be of benefit.

Global coordinated strategy for the progressive control of avian influenza

The response to the global AI threat must involve coordinated actions by international organisations, governmental agencies, poultry producers, scientific institutions, development partners and other stakeholders to prevent further spread of this virus. The response must aim to ensure the well-being of farmers, protect animal welfare and biodiversity, prevent economic losses, reduce poverty, ensure consumer confidence and allow further contribution of the poultry sector to global health, wealth, equity and sustainability. Regional and national AI control strategies should be based on best practices, appropriate enforcement of the legislation and close coordination with stakeholders from the public and private sectors. Members should increase their technical capacities and expertise, identify and use the relevant scientific knowledge, and engage in risk communication with relevant stakeholders.

Conclusions

The ecological and epidemiological changes resulting from the H5Nx 2.3.4.4b HPAI over the past three years have challenged the exclusivity of stamping-out programmes and require national Veterinary Services to work closely with wildlife and public health officials and other stakeholders to address this global One Health crisis. Critical strategic challenges to be addressed include surveillance and monitoring for early detection, prevention and establishing freedom from infection; improved disease control strategies, including increasing use of vaccination and specialised surveillance systems to demonstrate HPAI freedom in vaccinated flocks; implementation of international standards; and global coordination for the global control of HPAI.

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Défis stratégiques afférents au contrôle mondial de l'influenza aviaire de haute pathogénicité

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Résumé

Les souches virales de l'influenza aviaire de haute pathogénicité (IAHP) le plus souvent détectées dans le monde depuis 2005 sont des virus H5Nx appartenant à la lignée eurasienne A/Goose/Guangdong/1/96. La propagation de ces virus à travers le monde a provoqué une panzootie qui s'est étendue sur les six continents et représente une menace continue non seulement pour les volailles et les espèces sauvages et captives de l'avifaune, mais aussi pour les mammifères tant sauvages que captifs et domestiques, ainsi que pour les humains. L'écologie et l'épidémiologie de ces virus – en particulier le clade 2.3.4.4b – ont évolué et plus de 489 espèces sont désormais infectées, qui propagent le virus le long des routes migratoires. Cela se traduit par une mortalité élevée chez les oiseaux sauvages, espèces menacées incluses, en plus d'être une source de transmission vers les volailles et les mammifères. Il est indispensable que les secteurs en charge de la santé animale, la santé publique, la faune sauvage et l'environnement exercent une surveillance accrue et partagent leurs séquences virales de l'IAHP, ainsi que les métadonnées et les virus dont ils disposent, afin d'élucider la dynamique de l'infection au niveau des populations, condition essentielle pour faire face à ce défi majeur dans une optique « Une seule santé ». La conception de stratégies d'atténuation appropriées et la modification des pratiques d'élevage, de production et de vente peuvent réduire les risques d'introduction de ces virus dans les élevages, limiter leur amplification et évolution, et empêcher le retour de l'infection chez les oiseaux sauvages. La prévention et le contrôle de l'IAHP dans les pays où les virus 2.3.4.4b sont bien établis chez les volailles ou dans les zones exposées au risque d'introduction du virus via les populations d'oiseaux sauvages passent notamment par des mesures visant à contenir les effets de la maladie chez les volailles (renforcement de la biosécurité dans les élevages, vaccination, application du zonage et de la compartimentation). Leur mise en œuvre vient répondre à l'impasse que constituent une prévention fondée sur les seules mesures de biosécurité et un contrôle et élimination du virus fondés sur le seul abattage sanitaire. Le *Code sanitaire pour les animaux terrestres* de l'Organisation mondiale de la santé animale autorise la vaccination des volailles à certaines conditions sans que cela n'affecte le statut indemne d'IAHP, dès lors qu'une surveillance appropriée est exercée. La sécurité sanitaire des échanges internationaux de volailles et de produits d'origine aviaire est ainsi préservée. Néanmoins, l'application de la vaccination à plus large échelle se heurte toujours à la crainte de perdre de précieux marchés d'exportation.

Mots-clés

Compartimentation – Contrôle – H5N1 – Haute pathogénicité – Influenza aviaire – Prévention – Une seule santé – Vaccination – Vaccins – Zonage.

Desafíos estratégicos en el control mundial de la influenza aviar de alta patogenicidad

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Resumen

Los virus de la influenza aviar de alta patogenicidad (IAAP) de linaje euroasiático H5Nx A/Goose/Guangdong/1/96 han sido las principales cepas de IAAP detectadas a nivel mundial desde 2005. Estas se han diseminado por todo el mundo causando una panzootia que ha afectado seis continentes y ha amenazado de forma continua no solo a las aves silvestres, en cautividad o de corral, sino también a mamíferos silvestres, en cautividad y domésticos, así como al ser humano. La ecología y la epidemiología de los virus —y sobre todo del clado 2.3.4.4b— han cambiado, con más de 489 especies de aves infectadas que están propagando el virus a lo largo de las rutas migratorias. Esto provoca la muerte de muchas aves, incluidas especies en peligro de extinción, y sirve de vía de transmisión del virus a aves de corral y mamíferos. A fin de dilucidar la dinámica poblacional de las infecciones, lo que constituye un paso crucial para resolver este complejo problema vinculado al concepto «Una sola salud», es necesario mejorar la vigilancia y compartir información relativa a los virus causantes de la IAAP, sus secuencias y metadatos entre los sectores de la medicina veterinaria, la salud pública, la fauna silvestre y el medio ambiente. La elaboración de estrategias de mitigación adecuadas o la aplicación de cambios en las prácticas pecuarias, de producción y de comercialización pueden reducir el riesgo de introducción del virus en las explotaciones, así como su amplificación y evolución viral, y su posible propagación a las aves silvestres. Los enfoques para la prevención y el control de la IAAP en los países en los que estos virus 2.3.4.4b siguen arraigados en las aves de corral, o en lugares donde existe un riesgo de introducción del virus a través de las poblaciones de aves silvestres, consisten en medidas de reducción de los efectos de la enfermedad en las aves de corral (incluida la mejora de la bioseguridad de las explotaciones, la vacunación, la zonificación y la compartimentación). Su adopción refleja las dificultades que surgen al usar la bioseguridad como medida única para la prevención de la enfermedad, y el sacrificio sanitario cómo único método para el control y la eliminación del virus. El *Código Sanitario para los Animales Terrestres* de la Organización Mundial de Sanidad Animal autoriza el uso de la vacunación de las aves de corral en condiciones específicas y sin comprometer el estatus de ausencia de IAAP, siempre que se lleve a cabo una vigilancia adecuada, lo que favorece el comercio seguro de aves de corral y sus productos. No obstante, la preocupación por la pérdida de valiosos mercados de exportación sigue obstaculizando un mayor uso de la vacunación.

Palabras clave

Alta patogenicidad – Compartimentación – Control – H5N1 – Influenza aviar – Prevención – Una sola salud – Vacunación – Vacunas – Zonificación.

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