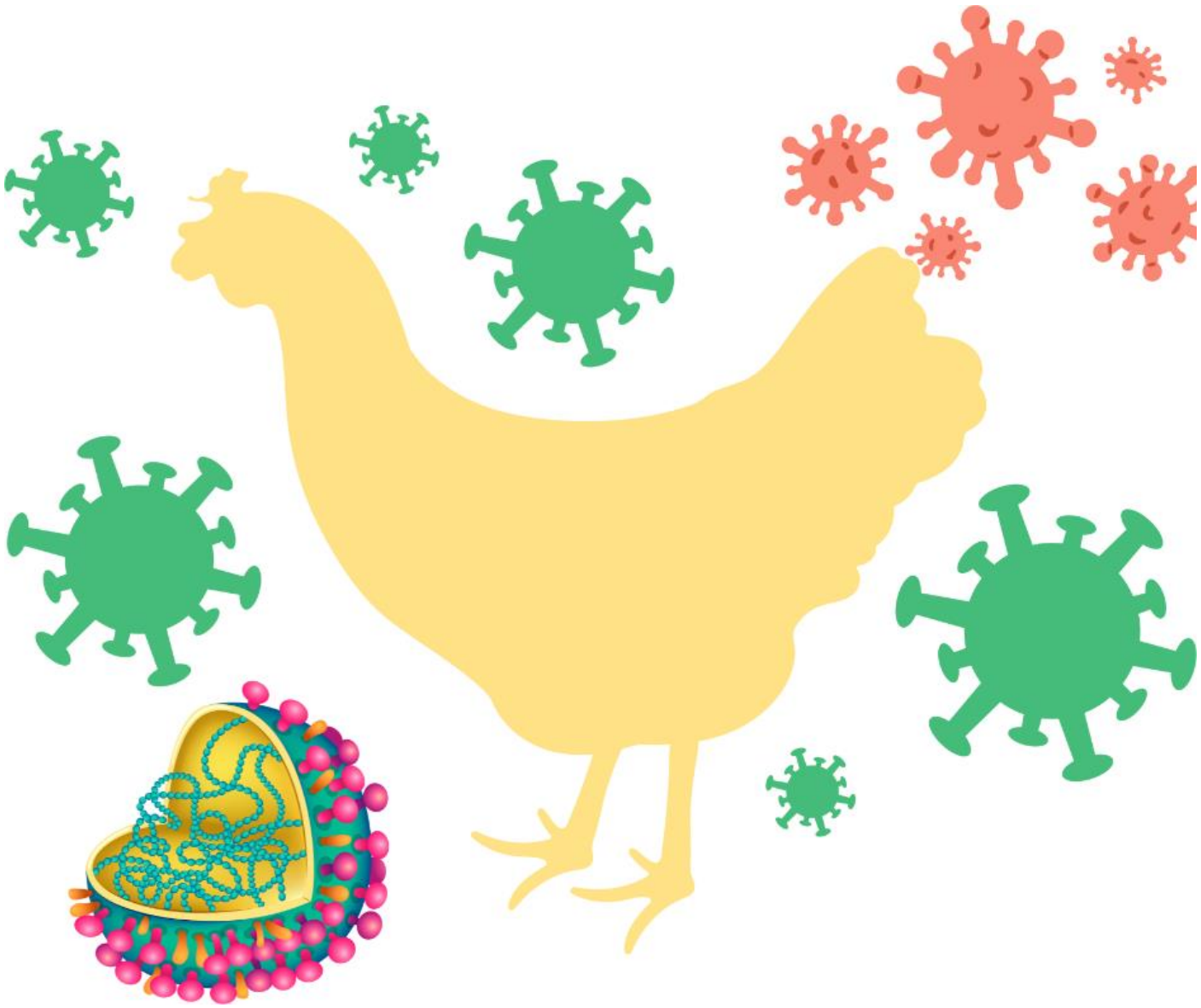
BIBLIOGRAFI

REVIEW AVIAN INFLUENZA TAHUN 2024



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Kata Pengantar

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Avian Influenza, sebagai salah satu penyakit yang memiliki dampak signifikan pada sektor peternakan dan kesehatan masyarakat, terus menjadi perhatian utama dalam dunia veteriner. Dengan perkembangan yang pesat terkait penelitian dan penemuan baru mengenai penyakit ini, penyusunan bibliografi ini diharapkan dapat mempermudah akses informasi dan membantu mendukung kajian lebih lanjut bagi para pemangku kepentingan.

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Akhir kata, kami mengucapkan terima kasih kepada semua pihak yang telah berkontribusi dalam penyusunan bibliografi ini. Semoga karya ini bermanfaat bagi seluruh pengguna.

Bogor, Oktober 2024

Perpustakaan Balai Besar Pengujian Standar Instrumen Veteriner
Badan Standardisasi Instrumen Pertanian, Kementerian Pertanian

DAFTAR ISI

1. **Highly pathogenic avian influenza A(H5N1) in animals: A systematic review and meta-analysis**, D. Katterine Bonilla-Aldana, Dayana M. Calle-Hernández, Juan R. Ulloque-Badaracco, Esteban A. Alarcón-Braga, Enrique A. Hernández-Bustamante, Juan C. Cabrera-Guzmán, Sthephanie M. Quispe-Vasquez, Miguel A. Huayta-Cortez, Vicente A. Benites-Zapata, Alfonso J. Rodriguez-Morales, New Microbes and New Infections, Volumes 60–61, 2024, 101439, https://doi.org/10.1016/j.nmni.2024.101439.

Abstract:

Introduction

Avian influenza A H5N1 is a significant global public health threat. Although relevant, systematic reviews about its prevalence in animals are lacking.

Methods

We performed a systematic literature review in bibliographic databases to assess the prevalence of H5N1 in animals. A meta-analysis with a random-effects model was performed to calculate the pooled prevalence and 95 % confidence intervals (95%CI). In addition, measures of heterogeneity (Cochran's Q statistic and I2 test) were reported.

Results

The literature search yielded 1359 articles, of which 33 studies were fully valid for analysis, including 96,909 animals. The pooled prevalence for H5N1 in birds (n = 90,045, 24 studies) was 5.0 % (95%CI: 4.0–6.0 %; I2 = 99.21); in pigs (n = 3,178, 4 studies) was 1.0 % (95%CI: 0.0–1.0 %); in cats (n = 2,911, 4 studies) was 0.0 % (95%CI: 0.0–1.0 %); and in dogs (n = 479, 3 studies) was 0.0 % (95%CI: 0.0–2.0 %).

Conclusions

While the occurrence of H5N1 in animals might be comparatively limited compared to other influenza viruses, its impact on public health can be substantial when it transmits to humans. This virus can potentially induce severe illness and has been linked to previous outbreaks. Therefore, it is essential to closely monitor and comprehend the factors influencing the prevalence of H5N1 in both avian and human populations to develop effective disease control and prevention strategies.

Keywords: *Avian influenza; Animals; Zoonotic; Outbreaks; Prevalence; Systematic review*

2. **The H4 subtype of avian influenza virus: a review of its historical evolution, global distribution, adaptive mutations and receptor binding properties**, Jing Liu, Zhaoping Liang, Wenchao Sun, Weiping Hua, Shujian Huang, Feng Wen, Poultry Science, Volume 103, Issue 8, 2024, 103913, https://doi.org/10.1016/j.psj.2024.103913.

Abstract:

The H4 subtype of avian influenza virus (AIV) exhibits a wide host range and is commonly found in migratory waterfowl. Recent studies have revealed that the H4N6 AIV can infect guinea pigs via aerosol transmission without

prior adaptation. Additionally, the Q226L/G228S substitutions in the receptor-binding site have led to structural changes in globular head of H4 AIV, resulting in a configuration similar to that of pandemic H2N2 and H3N2 human influenza viruses. This article provides an updated review of the historical evolution, global distribution, adaptive mutations, receptor-binding preferences, and host range of H4 AIV. The insights presented herein will help in assessing the potential risk of future H4 AIV epidemics.

Keywords: *Avian influenza; Avian influenza virus; H4Nx; H4N6; receptor binding*

3. **Preventive, safety and control measures against Avian Influenza A(H5N1) in occupationally exposed groups A scoping review** Haydee Susana Catalan Saenz, Liliana Cruz-Ausejo, One Health, Volume 19, 2024, 100766, https://doi.org/10.1016/j.onehlt.2024.100766.

Abstract:

Introduction

During the outbreak of avian influenza, A (H5N1) (IA) in wild and domestic birds recorded in January 2023, the epidemiological alert has been extended due to its potential contagion to humans, particularly in those exposed occupational groups.

Objective

to identify the primary occupational risk groups, as well as the preventive, safety, and control measures against IA intended or implemented in these positions.

Material and methods

A systematic search was conducted in Pubmed, Scopus, Web of science, Scielo and literature databases. Scientific articles, normative documents, and technical reports identifying vulnerable occupational groups and preventive measures against IA were included. Two authors conducted a full-text review, extracting information independently, and findings were summarized narratively.

Results

A total of 5518 documents were identified, and 30 reports were included. 20% of the reports were published in 2023, 13/30 were affiliated to a university institution. Occupationally exposed groups were identified both directly and indirectly. 63.3% of reports identified breeders, poultry farmers and sellers as the most concerning occupational group, while 60% identified biosecurity practices (use of PPE, handwashing) as the primary measure against IA, followed by strategies such as education (training and capacity-building).

Conclusion

Occupational groups of interest were identified, primarily those involved in sales, commerce, and the handling of bird waste with potential exposure to IA. Furthermore, the maintenance of biosecurity measures, cleaning-disinfection practices, and educational strategies in workplace settings are recommended.

Keywords: *Influenza A Virus; surveillance H5N1 subtype; Poultry; Population (MeSH term)*

4. **Re-evaluating efficacy of vaccines against highly pathogenic avian influenza virus in poultry: A systematic review and meta-analysis** IShin Tseng, Bing-Yi Pan, Yen-Chen Feng, Chi-Tai Fang, One Health, Volume18 , 2024, 100714, https://doi.org/10.1016/j.onehlt.2024.100714.

Abstract:

The global spread of highly pathogenic avian influenza (HPAI) A (H5N1) clade 2.3.4.4b virus since 2021 necessitates a re-evaluation of the role of vaccination in controlling HPAI outbreaks among poultry, which has been controversial because of the concern of silent spread with viral mutation and spillover to human. We systematically reviewed and meta-analyzed all existing data from experimental challenge trials to assess the efficacy of HPAI vaccines against mortality in specific pathogen free (SPF) chickens, with evaluation of the certainty of evidence (CoE) using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Out of 223 screened publications, 46 trials met our eligibility criteria. Inactivated vaccines showed an efficacy of 95% (risk ratio [RR] = 5% [95% CI: 1% to 17%], I2 = 0%, CoE high) against homologous strains and an efficacy of 78% (RR = 22% [95% CI: 14% to 37%], I2 = 18%, CoE high) against heterologous strains (test for subgroup difference p = 0.02). Live recombinant vaccines exhibited the highest efficacy at 97% (RR = 3% [95% CI: 1% to 13%], I2 = 0%, CoE high). Inactivated recombinant vaccines had an overall efficacy of 90% (RR = 10% [95% CI: 6% to 16%], I2 = 47%, CoE high). Commercial vaccines showed an overall efficacy of 91% (RR = 9% [95% CI: 5% to 17%], I2 = 23%, CoE high), with 96% efficacy (RR = 4% [95% CI: 1% to 21%], I2 = 0%, CoE high) against homologous strains and 90% efficacy (RR = 10% [95% CI: 5% to 20%], I2 = 31%, CoE moderate) against heterologous strains. Our systematic review offers an updated and unbiased assessment of vaccine efficacy against HPAI-related mortality, providing timely and crucial information for re-evaluating the role of vaccination in poultry avian influenza control policy amist the global HPAI outbreak post-2021.

Keywords: *Highly pathogenic avian influenza; HPAI; Vaccine; Vaccine efficacy; Meta-analysis*

5. **Control of highly pathogenic avian influenza through vaccination**, Xianying Zeng, Jianzhong Shi, Hualan Chen Journal of Integrative Agriculture, Volume 23, Issue 5, 2024, https://doi.org/10.1016/j.jia.2024.03.044.

Abstract:

The stamping-out strategy has been used to control highly pathogenic avian influenza viruses in many countries, driven by the belief that vaccination would not be successful against such viruses and fears that avian influenza virus in vaccinated birds would evolve more rapidly and pose a greater risk to humans. In this review, we summarize the successes in controlling highly pathogenic avian influenza in China and make suggestions regarding the requirements for vaccine selection and effectiveness. In addition, we present evidence that vaccination of poultry not only eliminates human infection with avian influenza virus, but also significantly reduces and abolishes some harmful characteristics of avian influenza virus.

Keywords: *avian influenza; control; highly pathogenic; vaccination*

6. **Avian Influenza outbreaks: Human infection risks for beach users - One health concern and environmental surveillance implications,** Ananda Tiwari, Päivi Meriläinen, Erika Lindh, Masaaki Kitajima, Pamela Österlund, Niina Ikonen, Carita Savolainen-Kopra, Tarja Pitkänen, Science of The Total Environment, Volume943, 2024, 173692, https://doi.org/10.1016/j.scitotenv.2024.173692.

Abstract:

Despite its popularity for water activities, such as swimming, surfing, fishing, and rafting, inland and coastal bathing areas occasionally experience outbreaks of highly pathogenic avian influenza virus (HPAI), including A(H5N1) clade 2.3.4.4b. Asymptomatic infections and symptomatic outbreaks often impact many aquatic birds, which increase chances of spill-over events to mammals and pose concerns for public health. This review examined the existing literature to assess avian influenza virus (AIV) transmission risks to beachgoers and the general population. A comprehensive understanding of factors governing such crossing of the AIV host range is currently lacking. There is limited knowledge on key factors affecting risk, such as species-specific interactions with host cells (including binding, entry, and replication via viral proteins hemagglutinin, neuraminidase, nucleoprotein, and polymerase basic protein 2), overcoming host restrictions, and innate immune response. AIV efficiently transmits between birds and to some extent between marine scavenger mammals in aquatic environments via consumption of infected birds. However, the current literature lacks evidence of zoonotic AIV transmission via contact with the aquatic environment or consumption of contaminated water. The zoonotic transmission risk of the circulating A(H5N1) clade 2.3.4.4b virus to the general population and beachgoers is currently low. Nevertheless, it is recommended to avoid direct contact with sick or dead birds and to refrain from bathing in locations where mass bird mortalities are reported. Increasing reports of AIVs spilling over to non-human mammals have raised valid concerns about possible virus mutations that lead to crossing the species barrier and subsequent risk of human infections and outbreaks.

Keywords*: Public health risks; Mutations; Reassortment; Spill-over; Pandemic potential; Genomic surveillance; Highly pathogenic avian influenza; H5N1*

7. **Genotypic and phenotypic susceptibility of emerging avian influenza A viruses to neuraminidase and cap-dependent endonuclease inhibitors,** Konstantin Andreev, Jeremy C. Jones, Patrick Seiler, Ahmed Kandeil, Richard J. Webby, Elena A. Govorkova, Antiviral Research, Volume 229, 2024, 105959, https://doi.org/10.1016/j.antiviral.2024.105959.

Abstract:

Avian influenza outbreaks, including ones caused by highly pathogenic A(H5N1) clade 2.3.4.4b viruses, have devastated animal populations and remain a threat to humans. Risk elements assessed for emerging influenza viruses include their susceptibility to approved antivirals. Here, we screened >20,000 neuraminidase (NA) or polymerase acidic (PA) protein sequences of potentially pandemic A(H5Nx), A(H7Nx), and A(H9N2) viruses that circulated globally in

2010–2023. The frequencies of NA or PA substitutions associated with reduced inhibition (RI) or highly reduced inhibition (HRI) by NA inhibitors (NAIs) (oseltamivir, zanamivir) or a cap-dependent endonuclease inhibitor (baloxavir) were low: 0.60% (137/22,713) and 0.62% (126/20,347), respectively. All tested subtypes were susceptible to NAIs and baloxavir at sub-nanomolar concentrations. A(H9N2) viruses were the most susceptible to oseltamivir, with IC50s 3- to 4-fold lower than for other subtypes (median IC50: 0.18 nM; n = 22). NA-I222M conferred RI of A(H5N1) viruses by oseltamivir (with a 26-fold IC50 increase), but NA-S246N did not reduce inhibition. PA-E23G, PA-K34R, PA-I38M/T, and the previously unreported PA-A36T caused RI by baloxavir in all subtypes tested. Avian A(H9N2) viruses endemic in Egyptian poultry predominantly acquired PA-I38V, which causes only a <3-fold decrease in the baloxavir EC50 and fails to meet the RI criteria. PA-E199A/D in A(H7Nx) and A(H9N2) viruses caused a 2- to 4-fold decrease in EC50 (close to the borderline for RI) and should be closely monitored. Our data indicate antiviral susceptibility is high among avian influenza A viruses with pandemic potential and present novel markers of resistance to existing antiviral interventions.

Keywords: *Avian influenza viruses; Antiviral susceptibility; Neuraminidase inhibitors; Oseltamivir; Zanamivir; Baloxavir*

8. **Highly pathogenic avian influenza A (H5N1) virus outbreak in Peru in 2022–2023,** Nieves Sevilla, Wendy Lizarraga, Victor Jimenez-Vasquez, Veronica Hurtado, Iris S. Molina, Lilian Huarca, Priscila Lope-Pari, Ivan Vargas, Gloria Arotinco, Carlos Padilla-Rojas, Infectious Medicine, Volume 3, Issue 2, 2024, 100108, https://doi.org/10.1016/j.imj.2024.100108.

Abstract:

An epizootic of highly pathogenic avian influenza A (H5N1) has spread worldwide since 2022. Even though this virus has been extensively studied for many decades, little is known about its evolution in South America.

Methods

Here, we describe the sequencing and characterization of 13 H5N1 genomes collected from wild birds, poultry, and wild mammals in Peru during the genomic surveillance of this outbreak.

Results

The samples belonged to the highly pathogenic avian influenza (H5N1) 2.3.4.4b clade. Chilean and Peruvian samples clustered in the same group and therefore share a common ancestor. An analysis of the hemagglutinin and neuraminidase genes detected new mutations, some dependent upon the host type.

Conclusions

The genomic surveillance of highly pathogenic avian influenza is necessary to promote the One Health policy and to overcome the new problems entailed by climate change, which may alter the habitats of resident and migratory birds.

Keywords: *Avian influenza A; H5N1; HPAI; Clade 2.3.4.4b; Sequencing; 2022–2023 outbreak*

9. **Avian influenza and gut microbiome in poultry and humans: A "One Health" perspective**, Ling Zhang, Erkai Zhou, Ce Liu, Xiaoyu Tian, Baode Xue, Kai Zhang, Bin Luo, Fundamental Research, Volume 4, Issue 3, 2024, Pages 455-462, https://doi.org/10.1016/j.fmre.2023.10.016.

Abstract:

A gradual increase in avian influenza outbreaks has been found in recent years. It is highly possible to trigger the next human pandemic due to the characteristics of antigenic drift and antigenic shift in avian influenza virus (AIV). Although great improvements in understanding influenza viruses and the associated diseases have been unraveled, our knowledge of how these viruses impact the gut microbiome of both poultry and humans, as well as the underlying mechanisms, is still improving. The "One Health" approach shows better vitality in monitoring and mitigating the risk of avian influenza, which requires a multi-sectoral effort and highlights the interconnection of human health with environmental sustainability and animal health. Therefore, monitoring the gut microbiome may serve as a sentinel for protecting the common health of the environment, animals, and humans. This review summarizes the interactions between AIV infection and the gut microbiome of poultry and humans and their potential mechanisms. With the presented suggestions, we hope to address the current major challenges in the surveillance and prevention of microbiome-related avian influenza with the "One Health" approach.

Keywords: *Avian influenza; AIV; Poultry; Gut microbiome; One Health; Poultry-Environment-Human Interface*

10. **Repeatability and reproducibility of hunter-harvest sampling for avian influenza virus surveillance in Great Britain,** Wesley Shemmings-Payne, Dilhani De Silva, Caroline J. Warren, Saumya Thomas, Marek J. Slomka, Scott M. Reid, Joe James, Ashley C. Banyard, Ian H. Brown, Alastair I. Ward, Research in Veterinary Science, Volume173, 2024, 105279, https://doi.org/10.1016/j.rvsc.2024.105279.

Abstract:

Emerging pathogens can threaten human and animal health, necessitating reliable surveillance schemes to enable preparedness. We evaluated the repeatability and reproducibility of a method developed previously during a single year at one study site. Hunter-harvested ducks and geese were sampled for avian influenza virus at three discrete locations in the UK. H5N1 highly pathogenic avian influenza (HPAIV) was detected in four species (mallard [Anas platyrhynchos], Eurasian teal [Anas crecca], Eurasian wigeon [Mareca penelope] and pink-footed goose [Anser brachyrhynchus]) across all three locations and two non-HPAIV H5N1, influenza A positive detections were made from a mallard and Eurasian wigeon at two locations. Virus was detected within 1-to-4 days of sampling at every location. Application of rapid diagnostic methods to samples collected from hunter-harvested waterfowl offers potential as an early warning system for the surveillance and monitoring of emerging and existing strains of avian influenza A viruses in key avian species.

Keywords: *Avian influenza; Disease surveillance; Highly pathogenic; anseriformes*

11. **Amplification of avian influenza virus circulation along poultry marketing chains in Bangladesh: A controlled field experiment,** Lisa Kohnle, Tridip Das, Md. Helal Uddin, Sanjib Chandra Nath, Md. Abu Shoieb Mohsin, Rashed Mahmud, Paritosh Kumar Biswas, Md. Ahasanul Hoque, Dirk Udo Pfeiffer, Guillaume Fournié, Preventive Veterinary Medicine, Volume 231, 2024, 106302, https://doi.org/10.1016/j.prevetmed.2024.106302.

Abstract:

The prevalence of avian influenza viruses is commonly found to increase dramatically as birds are transported from farms to live bird markets. Viral transmission dynamics along marketing chains are, however, poorly understood. To address this gap, we implemented a controlled field experiment altering chicken supply to a live bird market in Chattogram, Bangladesh. Broilers and backyard chickens traded along altered (intervention) and conventional (control) marketing chains were tested for avian influenza viruses at different time points. Upon arrival at the live bird market, the odds of detecting avian influenza viruses did not differ between control and intervention groups. However, 12 h later, intervention group odds were lower, particularly for broilers, indicating that viral shedding in live bird markets resulted partly from infections occurring during transport and trade. Curtailing avian influenza virus prevalence in live bird markets requires mitigating risk in marketing chain nodes preceding chickens' delivery at live bird markets.

Keywords: *avian influenza; H9N2; H5N1; poultry; live bird market; value chain*

12. **Increasing spillover of highly pathogenic avian influenza A (H5N1) virus to mammals,** Shao-Lun Zhai, Sheng-Nan Chen, Jieshi Yu, Bo Liu, Handuo Jia, New Microbes and New Infections, Volume 62, 2024, 101459, https://doi.org/10.1016/j.nmni.2024.101459.

Abstract

Influenza virus (IV), a segmented negative-sense RNA virus from the Orthomyxoviridae family, comprises four genera: Alphainfluenzavirus, Betainfluenzavirus, Gammainfluenzavirus, and Deltainfluenzavirus. The main species include Influenza A (IAV), B (IBV), C (ICV), and D (IDV), with IAV being the most diverse, featuring 18 hemagglutinin (HA) and 11 neuraminidase (NA) subtypes. IAV primarily affects over 100 bird species and various mammals, including humans, causing significant morbidity and mortality. Recent trends indicate an expanding host range for IAV, particularly with highly pathogenic avian influenza (HPAI) H5N1, which has recently been detected in cattle and goats in the U.S., marking a notable shift as these animals historically exhibited low susceptibility to IAVs. Infections in cattle have resulted in mild illness and decreased milk production. This emerging host adaptation highlights the need for enhanced vaccine immunization and viral surveillance to manage potential outbreaks and protect susceptible animal populations.

Keywords: *Cross-species transmission; H5N1 virus; Highly pathogenic avian influenza; Mammals; Spillover*.

13. **Human infection caused by avian influenza A (H10N5) virus,** Chih-Cheng Lai, Po-Ren Hsueh, Journal of Microbiology, Immunology and Infection, Volume 57, Issue 3, 2024, Pages 343-345, https://doi.org/10.1016/j.jmii.2024.04.006.

Abstract :

On January 27, 2024, a confirmed case of human infection with avian influenza A (H10N5) and seasonal influenza A (H3N2) was reported in Anhui Province, China, marking the first known instance of H10N5 in humans. The infected individual, a female farmer over 60 years old with underlying health conditions, developed symptoms on November 30, 2023, and tragically passed away on December 16, 2023. Investigations revealed her exposure to live poultry, with subsequent testing confirming H10N5 in stored duck meat. Surveillance efforts identified no additional cases, leading health authorities to classify the incident as an incidental cross-species transmission with a low risk of further infection. This case underscores the importance of ongoing research into the epidemiology and pathogenicity of H10N5, given its sporadic nature and potential for mutation. Recommendations for prevention include enhanced surveillance, public health advisories, and biosecurity measures in poultry management. The findings highlight the necessity for robust global monitoring to address emerging zoonotic threats.

Keywords: *H10N5, avian influenza, human infection, epidemiology, surveillance, public health, zoonotic disease, biosecurity.*

14. **Assessing avian influenza surveillance intensity in wild birds using a One Health lens,** Jolene A. Giacinti, Sarah J. Robinson, Christopher M. Sharp, Jennifer F. Provencher, David L. Pearl, Brian Stevens, Larissa Nituch, Rodney W. Brook, Claire M. Jardine, One Health, Volume 18, 2024, 100760, https://doi.org/10.1016/j.onehlt.2024.100760.

Abstract:

Wildlife disease surveillance, particularly for pathogens with zoonotic potential such as Highly Pathogenic Avian Influenza Virus (HPAIV), is critical to facilitate situational awareness, inform risk, and guide communication and response efforts within a One Health framework. This study evaluates the intensity of avian influenza virus (AIV) surveillance in Ontario's wild bird population following the 2021 H5N1 incursion into Canada. Analyzing 2562 samples collected between November 1, 2021, and October 31, 2022, in Ontario, Canada, we identify spatial variations in surveillance intensity relative to human population density, poultry facility density, and wild mallard abundance. Using the spatial scan statistic, we pinpoint areas where public engagement, collaborations with Indigenous and non-Indigenous hunter/harvesters, and working with poultry producers, could augment Ontario's AIV wild bird surveillance program. Enhanced surveillance at these human-domestic animal-wildlife interfaces is a crucial element of a One Health approach to AIV surveillance. Ongoing assessment of our wild bird surveillance programs is essential for strategic

planning and will allow us to refine approaches and generate results that continue to support the program's overarching objective of safeguarding the health of people, animals, and ecosystems.

Keywords: *Avian influenza virus; Wildlife disease surveillance; Migratory birds; One health; Wild birds; Poultry; Zoonotic pathogen surveillance*

15. **Genetic insertion of mouse Myxovirus-resistance gene 1 increases innate resistance against both high and low pathogenic avian influenza virus by significantly decreasing replication in chicken DF1 cell line,** Kelsey Briggs, Klaudia Chrzastek, Karen Segovia, Jongsuk Mo, Darrell R. Kapczynski, Virology, Volume 595, 2024, 110066, https://doi.org/10.1016/j.virol.2024.110066.

Abstract:

Avian influenza virus (AIV) is a constant threat to animal health with recent global outbreaks resulting in the death of hundreds of millions of birds with spillover into mammals. Myxovirus-resistance (Mx) proteins are key mediators of the antiviral response that block virus replication. Mouse (Mu) Mx (Mx1) is a strong antiviral protein that interacts with the viral nucleoprotein to inhibit polymerase function. The ability of avian Mx1 to inhibit AIV is unclear. In these studies, Mu Mx1 was stably introduced into chicken DF1 cells to enhance the immune response against AIV. Following infection, titers of AIV were significantly decreased in cells expressing Mu Mx1. In addition, considerably less cytopathic effect (CPE) and matrix protein staining was observed in gene-edited cells expressing Mu Mx1, suggesting Mu Mx1 is broadly effective against multiple AIV subtypes. This work provides foundational studies for use of gene-editing to enhance innate disease resistance against AIV.

Keywords: *Avian influenza; Mouse Mx1; Chickens; Replication; Gene-editing; Transgene*

16. **The risk of acquiring avian influenza from commercial poultry products and hen eggs: A qualitative assessment,** Erica Kintz, Wioleta J. Trzaska, Elaine Pegg, Wendy Perry, Alexander W. Tucker, Alec Kyriakides, Dragan Antic, Kathryn Callaghan, Anthony J. Wilson, Microbial Risk Analysis, Volumes 27–28, 2024, 100317, https://doi.org/10.1016/j.mran.2024.100317.

Abstract :

High pathogenicity and low pathogenicity avian influenza (HPAI and LPAI) viruses primarily infect birds, but they can also cause illness in other species, including humans. Some avian influenza (AI) strains can cause fatality rates of over 50 % in human infections. In October 2021, there was a substantial increase in the number of AI infections reported in birds in the UK. Given concerns that more infected and/or contaminated poultry products might reach retail, a risk assessment was performed to ensure that advice relating to the handling and consumption of these products remained appropriate.

The products considered in this risk assessment were commercial chicken and turkey products, farmed duck and geese products, and table eggs. The risk pathway included the likelihood animals or eggs from an infected flock would be sent for further processing, whether the resulting products would be released to retail after inspection, viral persistence during distribution and storage, and the ability of AI viruses to infect humans via the gastrointestinal route. The risk from any AI virus, not just the A(H5N1) strain that began circulating in 2021, was considered. Data was obtained from literature searches and FSA surveys.

The risk assessment determined that the likelihood of human infection with AI from poultry products for the UK population from handling and consuming commercial chicken or turkey products was **negligible** with **low uncertainty**, and for farmed duck and geese products was **very low** with **medium uncertainty**. The likelihood of infection for people in the UK from handling and consuming hen table eggs was **very low** with **low uncertainty.** The uncertainty rankings relate to the differing amounts of data available for each group of poultry products. The severity of illness in humans from AI infection was considered **high** with **medium** uncertainty. The conclusions of this risk assessment for UK consumers largely reflected advice and assessments from other countries and previous UK assessments. Given this, current guidance for handling and consuming poultry products was considered appropriate despite the increase in infections in birds during the 2021/22 and 2022/23 avian flu seasons. Since AI viruses were considered generally, these risk characterisations may need to be revisited based on evidence specific to a circulating virus to support risk management decisions.

Keywords : *Avian influenza; Qualitative risk assessment; Exposure assessment; Hazard characterization; Risk characterization; Commercial poultry; Eggs*

17. **Multiple transatlantic incursions of highly pathogenic avian influenza clade 2.3.4.4b A(H5N5) virus into North America and spillover to mammals,** Cassidy N.G. Erdelyan, Ahmed Kandeil, Anthony V. Signore, Megan E.B. Jones, Peter Vogel, Konstantin Andreev, Cathrine Arnason Bøe, Britt Gjerset, Tamiru N. Alkie, Carmencita Yason, Tamiko Hisanaga, Daniel Sullivan, Oliver Lung, Laura Bourque, Ifeoluwa Ayilara, Lemarie Pama, Trushar Jeevan, John Franks, Jeremy C. Jones, Jon P. Seiler, Lance Miller, Samira Mubareka, Richard J. Webby, Yohannes Berhane, Cell Reports, Volume 43, Issue 7, 2024, 114479, https://doi.org/10.1016/j.celrep.2024.114479.

Abstract:

Highly pathogenic avian influenza (HPAI) viruses have spread at an unprecedented scale, leading to mass mortalities in birds and mammals. In 2023, a transatlantic incursion of HPAI A(H5N5) viruses into North America was detected, followed shortly thereafter by a mammalian detection. As these A(H5N5) viruses were similar to contemporary viruses described in Eurasia, the transatlantic spread of A(H5N5) viruses was most likely facilitated by pelagic seabirds. Some of the Canadian A(H5N5) viruses from birds and mammals possessed the PB2-E627K substitution known to facilitate adaptation to mammals. Ferrets inoculated with A(H5N5) viruses showed rapid, severe disease onset, with some evidence of direct contact transmission. However, these viruses have maintained receptor binding traits of avian influenza viruses and were susceptible to oseltamivir and zanamivir. Understanding the factors influencing the virulence

and transmission of A(H5N5) in migratory birds and mammals is critical to minimize impacts on wildlife and public health.

Keywords: *avian influenza; HPAI; A(H5N5); clade 2.3.4.4b; Sable Island; wildlife transmission; antiviral susceptibility; contact transmission; ferret model*

18. **H5N1 avian influenza in USA: A call for vigilance in one health surveillance,** Ayush Anand, Mahendra Pratap Singh, Sanjit Sah, Amogh Verma, Mahalaqua Nazli Khatib, Manu Pant, Quazi Syed Zahiruddin, Sarvesh Rustagi, Clinical Infection in Practice, Volume 23, 2024, 100369, https://doi.org/10.1016/j.clinpr.2024.100369.

Abstract :

Avian influenza, particularly the H5N1 strain, remains a significant zoonotic threat, with recent cases underscoring its potential for human transmission. The first documented human infection with H5N1 in Texas was reported on April 1, 2024, following a prior case in Vietnam. This infection occurred in a dairy farm worker who developed conjunctivitis after exposure to infected cattle, marking a rare transmission route. Subsequent cases in Michigan involved two dairy workers with conjunctivitis, one confirmed positive for H5N1. Although no human-to-human transmission has been reported, the presence of H5N1 in U.S. dairy herds and wild birds raises concerns about broader exposure risks. The World Health Organization has indicated a low-to-moderate risk for exposed individuals but emphasizes the need for enhanced surveillance and a One Health approach, integrating human, animal, and environmental health strategies. Continuous monitoring and collaborative efforts are essential to mitigate potential zoonotic spillovers and prepare for future public health challenges.

Keywords: *USA; H5N1; Influenza; Avian influenza; Outbreak; zoonotic disease; conjunctivitis; One Health, surveillance; public health; animal health.*

19. **Baicalin reduced injury of and autophagy-related gene expression in RAW264.7 cells infected with H6N6 avian influenza virus,** Xin Yang, Junxian Li, Chunlan Shan, Xuqin Song, Jian Yang, Hao Xu, Deyuan Ou, Heliyon, Volume 10, Issue 12, 2024, e32645, https://doi.org/10.1016/j.heliyon.2024.e32645.

Abstract:

In the present study, we investigated whether baicalin could reduce the damage caused to RAW264.7 cells following infection with H6N6 avian influenza virus. In addition, we studied the expression of autophagy-related genes. The morphological changes in cells were observed by hematoxylin and eosin (H&E) staining, and the inflammatory factors in the cell supernatant were detected by enzyme-linked immunosorbent assay (ELISA). Transmission electron microscopy (TEM) was used to detect the levels of RAW264.7 autophagosomes, and western blotting and immunofluorescence were used to detect the protein expression of autophagy marker LC3. Quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) was used to detect the mRNA transcription levels of autophagy key factors. The results showed that different doses of baicalin significantly reduced the H6N6 virus-induced damage of

RAW264.7 cells. The contents of interleukin (IL)-1β, IL-2, IL-6, and tumor necrosis factor (TNF)-α in the cell supernatant significantly decreased. In addition, the protein expression of LC3 and Beclin-1, ATG12, ATG5 the mRNA levels were significantly decreased. This study showed that baicalin can reduce cell damage and affect the H6N6-induced autophagy level of RAW264.7 cells.

Keywords: *Baicalin; Influenza A virus; RAW264.7 cells; Autophagy; H6N6*

20. **Emergence of a human co-infected with seasonal influenza A (H3N2) virus and avian influenza A (H10N5) virus, China, December 2023,** Zimin Xie, Fengxiang Xu, Rongmao Chen, Ming Liao, Manman Dai, Journal of Microbiology, Immunology and Infection, 2024, https://doi.org/10.1016/j.jmii.2024.07.008.

Abstract:

High pathogenicity and low pathogenicity avian influenza (HPAI and LPAI) viruses primarily infect birds, but they can also cause illness in other species, including humans. Some avian influenza (AI) strains can cause fatality rates of over 50 % in human infections. In October 2021, there was a substantial increase in the number of AI infections reported in birds in the UK. Given concerns that more infected and/or contaminated poultry products might reach retail, a risk assessment was performed to ensure that advice relating to the handling and consumption of these products remained appropriate. The products considered in this risk assessment were commercial chicken and turkey products, farmed duck and geese products, and table eggs. The risk pathway included the likelihood animals or eggs from an infected flock would be sent for further processing, whether the resulting products would be released to retail after inspection, viral persistence during distribution and storage, and the ability of AI viruses to infect humans via the gastrointestinal route. The risk from any AI virus, not just the A(H5N1) strain that began circulating in 2021, was considered. Data was obtained from literature searches and FSA surveys. The risk assessment determined that the likelihood of human infection with AI from poultry products for the UK population from handling and consuming commercial chicken or turkey products was negligible with low uncertainty, and for farmed duck and geese products was very low with medium uncertainty. The likelihood of infection for people in the UK from handling and consuming hen table eggs was very low with low uncertainty. The uncertainty rankings relate to the differing amounts of data available for each group of poultry products. The severity of illness in humans from AI infection was considered high with medium uncertainty. The conclusions of this risk assessment for UK consumers largely reflected advice and assessments from other countries and previous UK assessments. Given this, current guidance for handling and consuming poultry products was considered appropriate despite the increase in infections in birds during the 2021/22 and 2022/23 avian flu seasons. Since AI viruses were considered generally, these risk characterisations may need to be revisited based on evidence specific to a circulating virus to support risk management decisions.

Keywords: *Emergence; H10N5; Cross-species transmission; Avian influenza virus*

21. **Evolutional dynamics of highly pathogenic avian influenza H5N8 genotypes in wintering bird habitats: Insights from South Korea's 2020–2021 season,** Young Jae Si, Seung-gyu Jang, Young-Il Kim, Mark Anthony B.

Casel, Dong-ju Kim, Ho Young Ji, Jeong Ho Choi, Ju Ryeon Gil, Rare Rollon, Hyunwoo Jang, So Youn Cheun, Eun-Ha Kim, Hyesung Jeong, Young Ki Choi, One Health, Volume 18, 2024, 100719, https://doi.org/10.1016/j.onehlt.2024.100719.

Abstract:

The winter of 2020–2021 in South Korea witnessed severe outbreaks of Highly Pathogenic Avian Influenza (HPAI) viruses, specifically multiple genotypes of the H5N8 subtype. These outbreaks prompted an extensive investigation into the genetic characteristics and evolutionary dynamics of these viruses. Under the auspices of the National Institute of Wildlife Disease Control and Prevention (NIWDC), we conducted a nationwide surveillance program, collecting 7588 specimens from diverse wild bird habitats. Influenza A viruses were isolated at a rate of 5.0%, with HPAI H5N8 viruses accounting for 38.5% of isolates, predominantly found in wild bird carcasses (97.3%). Genetic analysis revealed the emergence of novel HPAI genotypes due to genetic reassortment events. G1 and G2 viruses were separately introduced into Korea, with G1 viruses displaying dynamic behavior, resulting in diverse sub-genotypes (G1–1 to G1–5) and mainly isolated from clinical specimens. Conversely, the G2 virus, introduced later, became the dominant strain consistently isolated mainly from bird carcasses (88.9%). These findings underscore the emergence of numerous novel HPAI genotypes shaped by multiple reassortment events in high-density wintering grounds of migratory birds. These sites act as hotspots for genetic exchanges, significantly influencing avian ecology, including resident bird species, and contributing to HPAI H5N8 evolution. The genetic diversity and ongoing evolution of these viruses highlight the need for vigilant surveillance and adaptive control measures. Recognizing the potential spillover to human populations, a One Health approach is essential to mitigate the evolving threats posed by avian influenza.

Keywords: *HPAI H5N8 virus; Clade 2.3.4.4b; Reassortment; Genotypes; South Korea*

22. **Pacific and Atlantic sea lion mortality caused by highly pathogenic Avian Influenza A(H5N1) in South America,** Pablo I. Plaza, Víctor Gamarra-Toledo, Juan Rodríguez Euguí, Natalia Rosciano, Sergio A. Lambertucci, Travel Medicine and Infectious Disease, Volume 59, 2024, 102712, https://doi.org/10.1016/j.tmaid.2024.102712.

Abstract:

We describe the evolution of the outbreak of Highly Pathogenic Avian Influenza (HPAI) A(H5N1) in sea lions (Otaria flavescens) of South America. At least 24,000 sea lions died in Peru, Chile, Argentina, Uruguay, and Brazil between January–October 2023. The most plausible route of infection is cohabiting with or foraging on infected birds. However, we urge a detailed evaluation of the sea lions actual source of infection given that the concomitant massive wild bird mortalities registered in the Pacific Ocean did not occur in the Atlantic Ocean.

Keywords: *H5N1; Influenza; Mortality; Marine mammals; South America*

23. **Identification of broad-spectrum B-cell and T-cell epitopes of H9 subtype avian influenza virus HA protein using polypeptide scanning1,** Keji Quan, Nan Zhang, Mengqi Lin, Yuan Liu, Yue Li, Qun Hu, Maoshun Nie, Tao Qin, Jingzhi Li, Hongwei Ma, Sujuan Chen, Daxin Peng, Xiufan Liu, Journal of Integrative Agriculture, 2024, https://doi.org/10.1016/j.jia.2024.07.005.

Abstract:

The H9N2 subtype avian influenza virus (AIV) hemagglutinin (HA) protein is a major immunogen in which HA1 is a genetic variant and HA2 is relatively conserved. Identifying broad-spectrum antigen epitopes targeting HA1 is crucial for vaccine design and detection. Based on the phylogenetic and serological analyses, we identified 2 antigenic groups and 3 representative viruses: A/chicken/Jiangsu/JY040218C/2019, A/pigeon/Jiangsu/JY020616/2019, and A/chicken/Jiangsu/WX090312/2018. An overlapping peptide library was synthesized using HA1 amino acid sequences of the viruses as templates. Through peptide scanning of the sera against different strains of H9N2 subtype AIV, we identified peptides from 4 regions (H9-2/3, H9-20/21, H9-26, and H9-29/30/31) that demonstrated broad-spectrum reactivity. Immunological assay results demonstrated that H9-21 (219RIFKPLIGPRPLVNGLMGRI239), H9-26 (269SGESHGRILKTDLKMGSCTV289), and H9-30 (309YAFGNCPKYI GVKSLKLAVG329) effectively induced antibody generation and conferred partial protective efficacy against the parent virus JY040218C. The results of lymphocyte proliferation and ELISpot assays indicated that peptides H9-15 (159MRWLTQKNNAYPTQDAQYTN179), H9-22 (229PLVNGLMGRINYYWSVLKP G249), and H9-23 (239NYYWSVLKPGQTLRIKSDGN259) could effectively stimulate the expression of interferon-gamma in peripheral blood lymphocytes of chickens immunized against different strains of H9N2 AIV. Collectively, 5 novel cell epitopes H9-15, H9-22, H9-23, H9-26, and H9-30, including the best B cell epitope H9-26 and the best T cells epitope H9-22, were identified that could be targeted for vaccine design or detection approaches against H9N2 AIVs.

Keywords: *H9N2 subtype avian influenza virus; HA protein; Epitope; Microarray; Peptide*

24. **Spatiotemporal patterns of low and highly pathogenic avian influenza virus prevalence in murres in Canada from 2007 to 2022—a case study for wildlife viral monitoring**, Angela McLaughlin, Jolene Giacinti, Ishraq Rahman, Jordan Wight, Kathryn Hargan, Andrew S. Lang, Mark L. Mallory, Gregory J. Robertson, Kyle Elliot, Davor Ojkic, Stéphane Lair, Megan Jones, Yohannes Berhane, Grant Gilchrist, Laurie Wilson, Sabina I. Wilhelm, Michael G.C. Brown, Jennifer F. Provencher, Jian Liu, FACETS, Volume 9, 2024, Pages 1-13, https://doi.org/10.1139/facets-2023-0185.

Abstract:

Migratory seabirds move across ocean basins and are one of the primary reservoirs of low pathogenic avian influenza virus (LPAIV). This includes the millions of thick-billed murres (Uria lomvia) and common murres (Uria aalge) that are distributed across northern hemisphere oceans. In response to increasingly frequent detections of highly pathogenic avian influenza virus (HPAIV) in Europe in 2020–2021, avian influenza virus (AIV) monitoring in wildlife has increased. We compiled data from murres tested for AIV in Canada between 2007 and 2022 to quantify spatiotemporal

variation in the prevalence of LPAIV and HPAIV in these birds. No HPAIV was detected in murres prior to 2022, but HPAIV was present in 46% of both live/harvested and found dead murres in the northwestern Atlantic in 2022 with prevalence peaking at 63% among live birds in the summer. In the eastern Canadian Arctic, HPAIV prevalence in 2022 was <1% while LPAIV prevalence was 21%, which was significantly higher than previous sampling years. Power analyses suggest approximately 100 samples from breeding murres should be collected annually per colony or region to detect moderate changes in HPAIV prevalence. These analyses inform robust monitoring of viruses in wildlife, with implications for conservation, harvest management, and public health.

Keywords: *H5N1; highly pathogenic avian influenza virus; guillemots; seabirds; surveillance; wildlife monitoring*

25. **Avian influenza viruses in wild birds in Canada following incursions of highly pathogenic H5N1 virus from Eurasia in 2021–2022,** Jolene A. Giacinti, Anthony V. Signore, Megan E. B. Jones, Laura Bourque, Stéphane Lair, Claire Jardine, Brian Stevens, Trent Bollinger, Dayna Goldsmith, Margo Pybus, Iga Stasiak, Richard Davis, Neil Pople, Larissa Nituch, Rodney W. Brook, Davor Ojkic, Ariane Massé, Gabrielle Dimitri-Masson, Glen J. Parsons, Meghan Baker, Carmencita Yason, Jane Harms, Naima Jutha, Jon Neely, Yohannes Berhane, Oliver Lung, Shannon K. French, Lawrna Myers, Jennifer F. Provencher, Stephanie Avery-Gomm, Gregory J. Robertson, Tatsiana Barychka, Kirsty E. B. Gurney, Jordan Wight, Ishraq Rahman, Kathryn Hargan, Andrew S. Lang, William A. Montevecchi, Tori V. Burt, Michael G. C. Brown, Cynthia Pekarik, Trevor Thompson, Angela McLaughlin, Megan Willie, Laurie Wilson, Scott A. Flemming, Megan V. Ross, Jim Leafloor, Frank Baldwin, Chris Sharp, Hannah Lewis, Matthieu Beaumont, Al Hanson, Robert A. Ronconi, Eric Reed, Margaret Campbell, Michelle Saunders, Catherine Soos, mBio, Volume 15, Issue 8, 2024, https://doi.org/10.1128/mbio.03203-23.

Abstract:

Following the detection of novel highly pathogenic avian influenza virus (HPAIV) H5N1 clade 2.3.4.4b in Newfoundland, Canada, in late 2021, avian influenza virus (AIV) surveillance in wild birds was scaled up across Canada. Herein, we present the results of Canada's Interagency Surveillance Program for Avian Influenza in Wild Birds during the first year (November 2021–November 2022) following the incursions of HPAIV from Eurasia. The key objectives of the surveillance program were to (i) identify the presence, distribution, and spread of HPAIV and other AIVs; (ii) identify wild bird morbidity and mortality associated with HPAIV; (iii) identify the range of wild bird species infected by HPAIV; and (iv) genetically characterize detected AIV. A total of 6,246 sick and dead wild birds were tested, of which 27.4% were HPAIV positive across 12 taxonomic orders and 80 species. Geographically, HPAIV detections occurred in all Canadian provinces and territories, with the highest numbers in the Atlantic and Central Flyways. Temporally, peak detections differed across flyways, though the national peak occurred in April 2022. In an additional 11,295 asymptomatic harvested or live-captured wild birds, 5.2% were HPAIV positive across 3 taxonomic orders and 19 species. Whole-genome sequencing identified HPAIV of Eurasian origin as most prevalent in the Atlantic Flyway, along with multiple reassortants of mixed Eurasian and North American origins distributed across Canada, with moderate structuring at the flyway scale. Wild birds were victims and reservoirs of HPAIV H5N1 2.3.4.4b, underscoring the importance of surveillance encompassing samples from sick and dead, as well as live and harvested birds, to provide

insights into the dynamics and potential impacts of the HPAIV H5N1 outbreak. This dramatic shift in the presence and distribution of HPAIV in wild birds in Canada highlights a need for sustained investment in wild bird surveillance and collaboration across interagency partners.

IMPORTANCE

We present the results of Canada's Interagency Surveillance Program for Avian Influenza in Wild Birds in the year following the first detection of highly pathogenic avian influenza virus (HPAIV) H5N1 on the continent. The surveillance program tested over 17,000 wild birds, both sick and apparently healthy, which revealed spatiotemporal and taxonomic patterns in HPAIV prevalence and mortality across Canada. The significant shift in the presence and distribution of HPAIV in Canada's wild birds underscores the need for sustained investment in wild bird surveillance and collaboration across One Health partners.

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Keywords: *avian influenza; highly pathogenic avian influenza virus; H5N1; low pathogenicity avian influenza virus; wild birds; reservoir; surveillance*

26. **Mapping the risk of introduction of highly pathogenic avian influenza to Swedish poultry,** Pascale Stiles, Malin Grant, Hyeyoung Kim, Arianna Comin, Mikael Svensson, Johan Nilsson, Maria Nöremark, Preventive Veterinary Medicine, Volume 230, 2024, 106260, https://doi.org/10.1016/j.prevetmed.2024.106260.

Abstract:

Outbreaks of highly pathogenic avian influenza (HPAI) have resulted in severe economic impact for national governments and poultry industries globally and in Sweden in recent years. Veterinary authorities can enforce prevention measures, e.g. mandatory indoor housing of poultry, in HPAI high-risk areas. The aim of this study was to conduct a spatiotemporal mapping of the risk of introduction of highly pathogenic avian influenza virus (HPAIV) to Swedish poultry from wild birds, utilising existing data sources. A raster calculation method was used to assess the spatiotemporal risk of introduction of HPAIV to Swedish poultry. The environmental infectious pressure of HPAIV was first calculated in each 5 km by 5 km cell using four risk factors: density of selected species of wild birds, air temperature, presence of agriculture as land cover and presence of HPAI in wild birds based on data from October 2016-September 2021. The relative importance of each risk factor was weighted based on opinion of experts. The estimated environmental infectious pressure was then multiplied with poultry population density to obtain risk values for risk of introduction of HPAIV to poultry. The results showed a large variation in risk both on national and local level. The counties of Skåne and Östergötland particularly stood out regarding environmental infectious pressure, risk of

introduction to poultry and detected outbreaks of HPAI. On the other hand, there were counties, identified as having higher risk of introduction to poultry which never experienced any outbreaks. A possible explanation is the variation in poultry production types present in different areas of Sweden. These results indicate that the national and local variation in risk for HPAIV introduction to poultry in Sweden is high, and this would support more targeted compulsory prevention measures than what has previously been employed in Sweden. With the current and evolving HPAI situation in Europe and on the global level, there is a need for continuous updates to the risk map as the virus evolves and circulates in different wild bird species. The study also identified areas of improvement, in relation to data use and data availability, e.g. improvements to poultry registers, inclusion of citizen reported mortality in wild birds, data from standardised wild bird surveys, wild bird migration data as well as results from ongoing risk-factor studies.

Keywords: *Highly pathogenic avian influenza; Poultry; Risk mapping; Spatiotemporal modelling*

27. **Phylogeographic Dynamics of H9N2 Avian Influenza Viruses in Tunisia,** Imen Larbi, Marwa Arbi, Oussama Souiai, Halima Tougorti, Gary David Butcher, Jihene Nsiri, Chaima Badr, Imen EL Behi, Jihene Lachhab, Abdeljelil Ghram,Virus Research, Volume 344 ,2024, 199348, https://doi.org/10.1016/j.virusres.2024.199348.

Abstract:

Avian influenza virus subtype H9N2 is endemic in commercial poultry in Tunisia. This subtype affects poultry and wild birds in Tunisia and poses a potential zoonotic risk. Tunisian H9N2 strains carry, in their hemagglutinins, the human-like marker 226 L that is most influential in avian-to-human viral transmission. For a better understanding of how ecological aspects of the H9N2 virus and its circulation in poultry, migratory birds and environment shapes the spread of the dissemination of H9N2 in Tunisia, herein, we investigate the epidemiological, evolutionary and zoonotic potential of seven H9N2 poultry isolates and sequence their whole genome. Phylogeographic and phylodymanic analysis were used to examine viral spread within and among wild birds, poultry and environment at geographical scales. Genetic evolution results showed that the eight gene sequences of Tunisian H9N2 AIV were characterized by molecular markers involved with virulence and mammalian infections. The geographical distribution of avian influenza virus appears as a network interconnecting countries in Europe, Asia, North Africa and West Africa. The spatiotemporal dynamics analysis showed that the H9N2 virus was transmitted from Tunisia to neighboring countries notably Libya and Algeria. Interestingly, this study also revealed, for the first time, that there was a virus transmission between Tunisia and Morocco. Bayesian analysis showed exchanges between H9N2 strains of Tunisia and those of the Middle Eastern countries, analysis of host traits showed that duck, wild birds and environment were ancestry related to chicken. The subtypes phylodynamic showed that PB1 segment was under multiple inter-subtype reassortment events with H10N7, H12N5, H5N2 and H6N1 and that PB2 was also a subject of inter-subtype reassortment with H10N4.

Keywords: *Avian influenza; H9N2; Genetic analysis; Phylogeography, Tunisia*

28. **Molecular detection and characterization of highly pathogenic H5N1 clade 2.3.4.4b avian influenza viruses among hunter-harvested wild birds provides evidence for three independent introductions into Alaska,**

Andrew M. Ramey, Laura C. Scott, Christina A. Ahlstrom, Evan J. Buck, Alison R. Williams, Mia Kim Torchetti, David E. Stallknecht, Rebecca L. Poulson, Virology, Volume 589, 2024, 109938, https://doi.org/10.1016/j.virol.2023.109938.

Abstract:

We detected and characterized highly pathogenic avian influenza viruses among hunter-harvested wild waterfowl inhabiting western Alaska during September–October 2022 using a molecular sequencing pipeline applied to RNA extracts derived directly from original swab samples. Genomic characterization of 10 H5 clade 2.3.4.4b avian influenza viruses detected with high confidence provided evidence for three independent viral introductions into Alaska. Our results highlight the utility and some potential limits of applying molecular processing approaches directly to RNA extracts from original swab samples for viral research and monitoring.

Keywords: *Avian influenza; Bioinformatics; Bird flu; Highly pathogenic; Introduction; Molecular; Sequence*

29. **Baloxavir marboxil use for critical human infection of avian influenza A H5N6 virus,** Wenda Guan, Rong Qu, Lihan Shen, Kailin Mai, Weiqi Pan, Zhengshi Lin, Liping Chen, Ji Dong, Jiawei Zhang, Pei Feng, Yunceng Weng, Minfei Yu, Peikun Guan, Jinchao Zhou, Chuanmeizi Tu, Xiao Wu, Yang Wang, Chunguang Yang, Yun Ling, Sheng Le, Yangqing Zhan, Yimin Li, Xiaoqing Liu, Heyan Zou, Ziqi Huang, Hongxia Zhou, Qiubao Wu, Wenjie Zhang, Jiayang He, Teng Xu, Nanshan Zhong, Zifeng Yang, Med, Volume 5, Issue 1, 2024, Pages 32-41.e5, https://doi.org/10.1016/j.medj.2023.11.001.

Abstract:

Recent outbreaks of avian influenza and ongoing virus reassortment have drawn focus on spill-over infections. The increase in human infections with highly pathogenic avian influenza H5N6 virus and its high fatality rate posed a potential threat, necessitating the search for a more effective treatment.

Methods

Longitudinal clinical data and specimens were collected from five H5N6 patients after admission. All patients received antiviral treatment of either sequential monotherapy of oseltamivir and baloxavir or the two drugs in combination. Severity of illness; viral load in sputum, urine, and blood; and cytokine levels in serum and sputum were serially analyzed.

Findings

All patients developed acute respiratory distress syndrome (ARDS) and viral sepsis within 1 week after disease onset. When delayed oseltamivir showed poor effects, baloxavir was administered and rapidly decreased viral load. In addition, levels of IL-18, M-CSF, IL-6, and HGF in sputum and Mig and IL-18 in serum that reflected ARDS and sepsis deterioration, respectively, were also reduced with baloxavir usage. However, three patients eventually died from exacerbation of underlying disease and secondary bacterial infection. Nonsurvivors had more severe extrapulmonary organ dysfunction and insufficient H5N6 virus-specific antibody response.

Conclusions

For critical human cases of H5N6 infection, baloxavir demonstrated effects on viral load and pulmonary/extrapulmonary cytokines, even though treatment was delayed. Baloxavir could be regarded as a first-line treatment to limit continued viral propagation, with potential future application in avian influenza human infections and poultry workers exhibiting influenza-like illness.

Funding

This work was funded by the National Natural Science Foundation of China (81761128014).

Keywords: *avian influenza A(H5N6) virus; baloxavir marboxil; viral load; sepsis; cytokines*

30. **Global antigenic landscape and vaccine recommendation strategy for low pathogenic avian influenza A (H9N2) viruses,** Ke Zhai, Jinze Dong, Jinfeng Zeng, Peiwen Cheng, Xinsheng Wu, Wenjie Han, Yilin Chen, Zekai Qiu, Yong Zhou, Juan Pu, Taijiao Jiang, Xiangjun Du, Journal of Infection, Volume 89, Issue 2, 2024, 106199, https://doi.org/10.1016/j.jinf.2024.106199.

Abstract:

The sustained circulation of H9N2 avian influenza viruses (AIVs) poses a significant threat for contributing to a new pandemic. Given the temporal and spatial uncertainty in the antigenicity of H9N2 AIVs, the immune protection efficiency of vaccines remains challenging. By developing an antigenicity prediction method for H9N2 AIVs, named PREDAC-H9, the global antigenic landscape of H9N2 AIVs was mapped. PREDAC-H9 utilizes the XGBoost model with 14 well-designed features. The XGBoost model was built and evaluated to predict the antigenic relationship between any two viruses with high values of 81.1 %, 81.4 %, 81.3 %, 81.1 %, and 89.4 % in accuracy, precision, recall, F1 value, and area under curve (AUC), respectively. Then the antigenic correlation network (ACnet) was constructed based on the predicted antigenic relationship for H9N2 AIVs from 1966 to 2022, and ten major antigenic clusters were identified. Of these, four novel clusters were generated in China in the past decade, demonstrating the unique complex situation there. To help tackle this situation, we applied PREDAC-H9 to calculate the cluster-transition determining sites and screen out virus strains with the high cross-protective spectrum, thus providing an in silico reference for vaccine recommendation. The proposed model will reduce the clinical monitoring workload and provide a useful tool for surveillance and control of H9N2 AIVs.

Keywords: *Avian influenza; H9N2; Antigenic cluster; Surveillance; Vaccine recommendation*

31. **Inactivation of Avian Influenza Virus Inoculated into Ground Beef Patties Cooked on a Commercial Open-Flame Gas Grill,** John B. Luchansky, Anna C.S. Porto-Fett, David L. Suarez, Erica Spackman, Journal of Food Protection, Volume 87, Issue 8, 2024, 100325, https://doi.org/10.1016/j.jfp.2024.100325.

Abstract:

With the emergence of clade 2.3.4.4b H5N1 highly pathogenic avian influenza virus (AIV) infection of dairy cattle and its subsequent detection in raw milk, coupled with recent AIV infections affecting dairy farm workers, experiments were conducted to affirm the safety of cooked ground beef related to AIV because such meat is often derived from cull dairy cows. Specifically, retail ground beef (percent lean:fat = ca. 80:20) was inoculated with a low pathogenic AIV (LPAIV) isolate to an initial level of 5.6 log10 50% egg infectious doses (EID50) per 300 g patty. The inoculated meat was pressed into patties (ca. 2.54 cm thick, ca. 300 g each) and then held at 4 °C for up to 60 min. In each of the two trials, two patties for each of the following three treatments were cooked on a commercial open-flame gas grill to internal instantaneous temperatures of 48.9 °C (120°F), 62.8 °C (145°F), or 71.1 °C (160°F), but without any dwell time. Cooking inoculated ground beef patties to 48.9 °C (ave. cooking time of ca. 15 min) resulted in a mean reduction of ≥2.5 ± 0.9 log10 EID50 per 300 g of ground beef as assessed via quantification of virus in embryonating chicken eggs (ECEs). Likewise, cooking patties on a gas grill to 62.8 °C (ave. cooking time of ca. 21 min) or to the USDA FSIS recommended minimum internal temperature for ground beef of 71.1 °C (ave. cooking time of ca. 24 min) resulted in a reduction to nondetectable levels from initial levels of ≥5.6 log10 EID50 per 300 g. These data establish that levels of infectious AIV are substantially reduced within inoculated ground beef patties (20% fat) using recommended cooking procedures.

Keywords: *Attenuated vaccine strain; Avian influenza virus (AIV); Cooking; Ground beef; Low pathogenic avian influenza (LPAI) virus; Thermal inactivation*

32. **Genetic diversity of H5N1 and H5N2 high pathogenicity avian influenza viruses isolated from poultry in Japan during the winter of 2022–2023,** Yoshihiro Takadate, Junki Mine, Ryota Tsunekuni, Saki Sakuma, Asuka Kumagai, Hayate Nishiura, Kohtaro Miyazawa, Yuko Uchida, Virus Research, Volume 347, 2024, 199425, https://doi.org/10.1016/j.virusres.2024.199425.

Abstract:

High pathogenicity avian influenza viruses (HPAIVs) of the H5N1 and H5N2 subtypes were responsible for 84 HPAI outbreaks on poultry premises in Japan during October 2022–April 2023. The number of outbreaks during the winter of 2022–2023 is the largest ever reported in Japan. In this study, we performed phylogenetic analyses using the full genetic sequences of HPAIVs isolated in Japan during 2022–2023 and those obtained from a public database to identify their genetic origin. Based on the hemagglutinin genes, these HPAIVs were classified into the G2 group of clade 2.3.4.4b, whose ancestors were H5 HPAIVs that circulated in Europe in late 2020, and were then further divided into three subgroups (G2b, G2d, and G2c). Approximately one-third of these viruses were classified into the G2b and G2d groups, which also included H5N1 HPAIVs detected in Japan during 2021–2022. In contrast, the remaining two-thirds were classified into the G2c group, which originated from H5N1 HPAIVs isolated in Asian countries and Russia during the winter of 2021–2022. Unlike the G2b and G2d viruses, the G2c viruses were first detected in Japan in the fall of 2022. Importantly, G2c viruses caused the largest number of outbreaks throughout Japan over the longest period during the season. Phylogenetic analyses using eight segment genes revealed that G2b, G2d, and G2c viruses were divided into 2, 4, and 11 genotypes, respectively, because they have various internal genes closely related to those of avian influenza

viruses detected in wild birds in recent years in Asia, Russia, and North America, respectively. These results suggest that HPAIVs were disseminated among migratory birds, which may have generated numerous reassortant viruses with various gene constellations, resulting in a considerable number of outbreaks during the winter of 2022–2023.

Keywords: *High pathogenicity avian influenza virus; Poultry; Phylogenetic analysis; H5N1; H5N2; Winter of 2022–2023*

33. **Isolation and genetic characterization of multiple genotypes of both H5 and H7 avian influenza viruses from environmental water in the Izumi plain, Kagoshima prefecture, Japan during the 2021/22 winter season,** Kosuke Okuya, Mana Esaki, Kaori Tokorozaki, Taichi Hasegawa, Makoto Ozawa, Comparative Immunology, Microbiology and Infectious Diseases, Volume 109, 2024, 102182, https://doi.org/10.1016/j.cimid.2024.102182.

Abstract:

In the 2021/22 winter, one H5N1 and nine H5N8 high pathogenicity avian influenza viruses (HPAIVs) of clade 2.3.3.4b were isolated from the water in crane roosts on the Izumi plain, Japan. Additionally, we isolated low pathogenicity avian influenza viruses (LPAIVs) of five subtypes: H1N1, H4N2, H4N6, H7N7, and H10N4. H5N8 HPAIVs belonging to the G2a group were isolated throughout winter, whereas H5N1 HPAIV belonging to the G2b group were isolated only in early winter. These findings suggest co-circulation of both G2a and G2b HPAIVs in early winter. Although two H7N7 LPAIVs were isolated from cranes' roost water collected on the same day, the gene constellations of the two isolates were clearly different, indicating the contemporary invasion of at least two different genotypes of H7N7 LPAIVs in the Izumi plain. This study underscores the importance of monitoring both HPAIVs and LPAIVs to understand avian influenza virus ecology in migratory waterfowl populations.

Keywords: *High pathogenicity avian influenza virus; Environmental water; Phylogenetic analysis; Multiple genotypes*

34. **H5N1 avian influenza virus PB2 antagonizes duck IFN-β signaling pathway by targeting mitochondrial antiviral signaling protein1,** Zuxian Chen, Bingbing Zhao, Yingying Wang, Yuqing Du, Siyu Feng, Junsheng Zhang, Luxiang Zhao, Weiqiang Li, Yangbao Ding, Peirong Jiao, Journal of Integrative Agriculture, 2024, https://doi.org/10.1016/j.jia.2023.12.040.

Abstract:

Type I interferon (IFN)-mediated innate immune responses represent the first line of host defense against viral infection. However, the molecular mechanisms by which avian influenza virus (AIV) inhibits type I IFN production in ducks are not well understood. Here, we first found that the polymerase basic 2 (PB2) protein of H5N1 subtype AIV inhibited the type I IFN responses by targeting duck mitochondrial antiviral signaling protein (MAVS). We further demonstrated that H5N1-PB2 bound to the △transmembrane (△TM) domain of duck MAVS, and the polymerase basic 1 (PB1) binding

domain (PBD) and RNA binding nuclear import domain (RND) of H5N1-PB2 interacted with MAVS to inhibit type I IFN expression in ducks. Collectively, our findings contribute to understanding the molecular mechanism by which AIV proteins regulate the retinoic acid-inducible gene I (RIG-I)-like receptor (RLR) signaling pathway to evade host antiviral immune responses in ducks.

Keywords: *avian influenza virus; polymerase basic 2; mitochondrial antiviral signaling protein; duck; type I interferon*

35. **Immunogenicity and protective efficacy of a multivalent herpesvirus vectored vaccine against H9N2 low pathogenic avian influenza in chicken,** Fiona Ingrao, Eva Ngabirano, Fabienne Rauw, Gwenaëlle Dauphin, Bénédicte Lambrecht, Vaccine, Volume 42, Issue 15, 2024, Pages 3410-3419, https://doi.org/10.1016/j.vaccine.2024.04.038.

Abstract:

The application of recombinant herpesvirus of turkey, expressing the H9 hemagglutinin gene from low pathogenic avian influenza virus (LPAIV) H9N2 and the avian orthoavulavirus-1 (AOAV-1) (commonly known as Newcastle Disease virus (NDV)) fusion protein (F) as an rHVT-H9-F vaccine, is an alternative to currently used classical vaccines. This study investigated H9- and ND-specific humoral and mucosal responses, H9-specific cell-mediated immunity, and protection conferred by the rHVT-H9-F vaccine in specific pathogen-free (SPF) chickens. Vaccination elicited systemic NDV F- and AIV H9-specific antibody response but also local antibodies in eye wash fluid and oropharyngeal swabs. The ex vivo H9-specific stimulation of splenic and pulmonary T cells in the vaccinated group demonstrated the ability of vaccination to induce systemic and local cellular responses. The clinical protection against a challenge using a LPAIV H9N2 strain of the G1 lineage isolated in Morocco in 2016 was associated with a shorter duration of shedding along with reduced viral genome load in the upper respiratory tract and reduced cloacal shedding compared to unvaccinated controls.

Keywords: *Vaccine; Avian influenza; Herpesvirus of turkey; Chicken; Cell-mediated immunity; Mucosal immunity*

36. **Evolutionary dynamics and comparative pathogenicity of clade 2.3.4.4b H5 subtype avian influenza viruses, China, 2021–2022,** Siru Lin, Junhong Chen, Ke Li, Yang Liu, Siyuan Fu, Shumin Xie, Aimin Zha, Aiguo Xin, Xinyu Han, Yuting Shi, Lingyu Xu, Ming Liao, Weixin Jia, Virologica Sinica, Volume 39, Issue 3, 2024, Pages 358-368, https://doi.org/10.1016/j.virs.2024.04.004.

Abstract:

The recent concurrent emergence of H5N1, H5N6, and H5N8 avian influenza viruses (AIVs) has led to significant avian mortality globally. Since 2020, frequent human-animal interactions have been documented. To gain insight into the novel H5 subtype AIVs (i.e., H5N1, H5N6 and H5N8), we collected 6102 samples from various regions of China between January 2021 and September 2022, and identified 41 H5Nx strains. Comparative analyses on the evolution and

biological properties of these isolates were conducted. Phylogenetic analysis revealed that the 41 H5Nx strains belonged to clade 2.3.4.4b, with 13 related to H5N1, 19 to H5N6, and 9 to H5N8. Analysis based on global 2.3.4.4b viruses showed that all the viruses described in this study were likely originated from H5N8, exhibiting a heterogeneous evolutionary history between H5N1 and H5N6 during 2015–2022 worldwide. H5N1 showed a higher rate of evolution in 2021–2022 and more sites under positive selection pressure in 2015–2022. The antigenic profiles of the novel H5N1 and H5N6 exhibited notable variations. Further hemagglutination inhibition assay suggested that some A(H5N1) viruses may be antigenically distinct from the circulating H5N6 and H5N8 strains. Mammalian challenge assays demonstrated that the H5N8 virus (21GD001_H5N8) displayed the highest pathogenicity in mice, followed by the H5N1 virus (B1557_H5N1) and then the H5N6 virus (220086_H5N6), suggesting a heterogeneous virulence profile of H5 AIVs in the mammalian hosts. Based on the above results, we speculate that A(H5N1) viruses have a higher risk of emergence in the future. Collectively, these findings unveil a new landscape of different evolutionary history and biological characteristics of novel H5 AIVs in clade 2.3.4.4b, contributing to a better understanding of designing more effective strategies for the prevention and control of novel H5 AIVs.

Keywords: *Avian influenza virus (AIV); H5 subtypes AIVs; Evolutionary; Pathogenicity*

37. **Phylodynamics of avian influenza A(H5N1) viruses from outbreaks in Brazil,** Anselmo Vasconcelos Rivetti, Dilmara Reischak, Cairo Henrique Sousa de Oliveira, Juliana Nabuco Pereira Otaka, Christian Steffe Domingues, Talita de Lima Freitas, Fernanda Gomes Cardoso, Lucas Oliveira Montesino, Ana Luiza Savioli da Silva, Soraya Cecília Albieri Camillo, Fernanda Malta, Deyvid Amgarten, Aristóteles Goés-Neto, Eric Roberto Guimarães Rocha Aguiar, Iassudara Garcia de Almeida, Carla Amaral Pinto, Antônio Augusto Fonseca, Marcelo Fernandes Camargos, Virus Research, Volume 347, 2024, 199415, https://doi.org/10.1016/j.virusres.2024.199415.

Abstract:

Our study identified strains of the A/H5N1 virus in analyzed samples of subsistence poultry, wild birds, and mammals, belonging to clade 2.3.4.4b, genotype B3.2, with very high genetic similarity to strains from Chile, Uruguay, and Argentina. This suggests a migratory route for wild birds across the Pacific, explaining the phylogenetic relatedness. The Brazilian samples displayed similarity to strains that had already been previously detected in South America. Phylogeographic analysis suggests transmission of US viruses from Europe and Asia, co-circulating with other lineages in the American continent. As mutations can influence virulence and host specificity, genomic surveillance is essential to detect those changes, especially in critical regions, such as hot spots in the HA, NA, and PB2 sequences. Mutations in the PB2 gene (D701N and Q591K) associated with adaptation and transmission in mammals were detected suggesting a potential zoonotic risk. Nonetheless, resistance to neuraminidase inhibitors (NAIs) was not identified, however, continued surveillance is crucial to detect potential resistance. Our study also mapped the spread of the virus in the Southern hemisphere, identifying possible entry routes and highlighting the importance of surveillance to prevent outbreaks and protect both human and animal populations.

Keywords: *Highly pathogenic avian influenza virus; Outbreaks; Complete genetic characterization, Phylodynamics, Point mutations*

38. **Effects of adding antibiotics to an inactivated oil-adjuvant avian influenza vaccine on vaccine characteristics and chick health,** Xuehuai Shen, Anyun Zhang, Ruihong Zhao, Lei Yin, Dongdong Yin, Yin Dai, Hongyan Hou, Jieru Wang, Xiaomiao Hu, Xiaocheng Pan, Danjun Zhang, Wei Liu, Yongjie Liu, Kai zhan, Poultry Science, Volume 103, Issue 10, 2024, 104135, https://doi.org/10.1016/j.psj.2024.104135.

Abstract:

During poultry immunization, antibiotics are typically added to inactivated oil-adjuvant avian influenza (AI) vaccines. Here, we evaluated the effects of adding ceftiofur, a third-generation cephalosporin, to an AI vaccine on vaccine stability and structure and on chick growth, immune efficacy, blood concentrations, biochemical and immunological indices, and gut microbiota. The results demonstrated that neither aqueous ceftiofur sodium nor ceftiofur hydrochloride oil emulsion formed a stable mixture with the vaccine. Adding ceftiofur formulations, particularly ceftiofur hydrochloride, at >4% significantly destabilized the vaccine's water-in-oil structures. Adding ceftiofur also increased vaccine malabsorption at the injection site; specifically, adding ceftiofur hydrochloride reduced H5N8 and H7N9 antibody titers after the first immunization ($P < 0.05$) and H7N9 antibody titers after the second immunization ($P < 0.01$). Serum drug concentrations did not differ significantly between the groups with ceftiofur sodium and hydrochloride addition. Ceftiofur addition increased postvaccination chick weight loss; compared with the vaccine alone, ceftiofur sodium–vaccine mixture increased chick weight significantly ($P < 0.05$). Ceftiofur addition also increased stress indices and reduced antioxidant capacity significantly ($P < 0.05$ or $P < 0.01$). Vaccination-related immune stress reduced gut microbiota diversity in chicks; ceftiofur addition reversed this change. AI vaccine immunization significantly reduced the relative abundance of Lactobacillus and Muribaculaceae but significantly increased that of Bacteroides and Eubacterium coprostanoligenes group. Ceftiofur addition restored the gut microbiota structure; in particular, ceftiofur hydrochloride addition significantly increased the abundance of the harmful gut microbes Escherichia-Shigella and Enterococcus, whereas ceftiofur sodium addition significantly reduced it. The changes in gut microbiota led to alterations in metabolic pathways related to membrane transport, amino acids, and carbohydrates. In conclusion, adding ceftiofur to the AI vaccine had positive effects on chick growth and gut microbiota modulation; however, different antibiotic concentrations and formulations may disrupt vaccine structure, possibly affecting vaccine safety and immunization efficacy. Thus, the addition of antibiotics to oil-adjuvant vaccines is associated with a risk of immunization failure and should be applied to poultry with caution.

Keywords: *avian influenza vaccines; antibiotic; immunization effect; drug concentration; chick health*

39. **Efficacy of live and inactivated recombinant Newcastle disease virus vaccines expressing clade 2.3.4.4b H5 hemagglutinin against H5N1 highly pathogenic avian influenza in SPF chickens, Broilers, and domestic ducks,** Deok-Hwan Kim, Seung-hun Lee, Jiwon Kim, Jiho Lee, Jei-hyun Jeong, Ji-yun Kim, Seung-un Song, Hyukchae Lee, Andrew Y Cho, Ji-Yeon Hyeon, Sungsu Youk, Chang-Seon Song, Vaccine, Volume 42, Issue 18, 2024, Pages 3756-3767, https://doi.org/10.1016/j.vaccine.2024.04.088.

Abstract:

A Newcastle disease virus (NDV)-vectored vaccine expressing clade 2.3.4.4b H5 Hemagglutinin was developed and assessed for efficacy against H5N1 highly pathogenic avian influenza (HPAI) in specific pathogen-free (SPF) chickens, broilers, and domestic ducks. In SPF chickens, the live recombinant NDV-vectored vaccine, rK148/22-H5, achieved complete survival against HPAI and NDV challenges and significantly reduced viral shedding. Notably, the live rK148/22-H5 vaccine conferred good clinical protection in broilers despite the presence of maternally derived antibodies. Good clinical protection was observed in domestic ducks, with decreased viral shedding. It demonstrated complete survival and reduced cloacal viral shedding when used as an inactivated vaccine from SPF chickens. The rK148/22-H5 vaccine is potentially a viable and supportive option for biosecurity measure, effectively protecting in chickens against the deadly clade 2.3.4.4b H5 HPAI and NDV infections. Furthermore, it aligns with the strategy of Differentiating Infected from Vaccinated Animals (DIVA).

Keywords: *High pathogenic avian influenza; H5N1 clade 2.3.4.4b; Newcastle disease virus-vectored vaccine; Broiler maternally-derived antibodies; Domestic ducks*

40. **The avian influenza A virus receptor SA-α2,3-Gal is expressed in the porcine nasal mucosa sustaining the pig as a mixing vessel for new influenza viruses,** Charlotte Kristensen, Lars E. Larsen, Ramona Trebbien, Henrik E. Jensen Virus Research, Volume 340, 2024, 199304, https://doi.org/10.1016/j.virusres.2023.199304.

Abstract:

Influenza A viruses (IAVs) originate from wild birds but have on several occasions jumped host barriers and are now also circulating in humans and mammals. The IAV host receptors (glycans with galactose linked to a sialic acid (SA) in an α2,3 or α2,6 linkage) are crucial host factors restricting inter-species transmission. In general, avian-origin IAVs show a preference for SA-α2,3 (avian receptor), whereas IAVs isolated from humans and pigs prefer SA-α2,6 (human receptor). N-acetylneuraminic acid (Neu5Ac) and N-glycolylneuraminic acid (Neu5Gc) are the two major SAs. Neu5Ac is expressed in all species, whereas Neu5Gc is only expressed in a limited number of domestic species such as pigs and horses, but not in humans. Despite that previous studies have shown that the IAV host receptor distribution appears to be similar in pigs and humans, none of these studies have investigated the expression of Neu5Gc-α2,6 in situ in porcine tissues. Thus, the aim of this study was to elucidate the distribution of IAV host receptors expressed in the porcine respiratory tract and relate the expression to the viral tropism of diverse host-adapted IAVs. The IAV receptor (SA-α2,3 and SA-α2,6) distribution and the presence of specifically Neu5Gc-α2,6 in the porcine nasal, tracheal, and lung tissues was investigated by lectin histochemistry. Furthermore, IAV immunohistochemistry was performed on tissues from pigs experimentally infected with IAVs, either adapted to pigs or humans, to investigate the significance of the IAV host receptors and the tropism of the diverse host-adapted IAVs. We document for the first time the expression of the avian receptor on the surface of the porcine nasal mucosa and an equal expression of Neu5Ac-α2,6 and Neu5Gc-α2,6 on the surface of the tracheal epithelium and alveoli. In all IAV-infected pigs, we found a low amount of IAV-positive cells in the trachea despite a high expression of the human receptor. Cumulatively, these findings suggest that optimal IAV

replication involves a complex interplay between the viruses and their host receptors and that there might be other less clearly defined host factors that determine the site of replication.

Keywords: *Influenza A virus; Host tropism; Sialic acid; Experimental infections; Receptor; Pigs*

41. **Spread of avian influenza among poultry specialists in England during winter 2022/23: National poultry housing order and environmental drivers,** Peter Tammes, Dialogues in Health, Volume 4, 2024, 100165, https://doi.org/10.1016/j.dialog.2024.100165.

Abstract:

To examine the impact of the national poultry housing order the UK government introduced on 7 November 2022 on the spreading of the avian influenza virus among poultry premises.

Methods

A longitudinal design with 15 weeks of infected poultry specialist incidence rates per 100 poultry specialists during the 2022/23 winter for 8 English regions. A multilevel regression model was used to analyse repeated measurements. Time was level-1 unit and regions level-2 unit resulting in 120 observations. Random intercept models included interactions between housing order and weekly infected wild birds, poultry density, or weekly average temperatures divided into terciles. In models where these variables were not included as an interaction term they were introduced as confounders.

Results

After the introduction of the housing order, it took 3 weeks for a considerable reduction in poultry specialist incidence rates. Reduction in incidence rates was strongest in regions with highest poultry density, from 1.27 (95%CI 0.99 to 1.56) to 0.30 (95%CI 0.09 to 0.52). Considerable reductions were also seen in regions with most detected infected wild birds.

Conclusion

The housing order was successful in reducing infected poultry specialist incidence rates three weeks after its introduction. Strongest impact in regions with highest poultry density.

Keywords: *Virus surveillance; avian influenza; outbreak; epidemiology; housing order; England*

42. **Application of glass box AI to large numbers of medical records for rapid response to future respiratory virus pandemics. Examples considering potential future high-fatality COVID strains and a potential avian influenza pandemic in humans,** B. Robson, O.K. Baek, Informatics in Medicine Unlocked, Volume 46, 2024, 101454, https://doi.org/10.1016/j.imu.2024.101454.

Abstract:

It is crucial to consider the consequences that new strains of respiratory viruses such as COVID-19 and avian influenza could have on humans. Possible future human-to-human transmission of avian influenza is of particular concern. As discussed, not all countries took a worst-case approach to COVID-19 at the outset, with regrettable outcomes. To better

prepare, it is important to have access to as much information as possible, including digital patient records, and to use that information in a timely fashion so that appropriate actions can be taken early. A glass-box AI approach, complementary to current mainly black-box AI, can effectively manage uncertainty, missing data, and feature interactions in a probabilistic fashion. This approach can obtain standard epidemiological measures, discover unexpected demographic and clinical interactions in past data, and then apply them to small amounts of future data. As this concerns future response, this is primarily a review and position paper. It is emphasized that our results at both the quantitative and qualitative levels are based on models for future pandemics of unknown nature and possibly great severity and are not intended to be realistic. We may sometimes overemphasize severity, but that is a worst-case strategy. We do not consider all epidemiological modeling methods. Rather, this paper concerns how some simple, less variant measures from the first COVID-19 wave and more general qualitative information might be used in combination with analysis of rapidly updated patient records in the first few days of the first wave of a future pandemic.

Keywords: *Pandemics; Epidemics; Patient medicial records; Longtitudinal health records; Early response; Epidemiology*

43. **Dramatic re-emergence of avian influenza in Colombia and Latin America,** Daniela Paternina, Rene Herazo, Misael Oviedo, Salim Mattar, Travel Medicine and Infectious Disease, Volume 59, 2024, 102711, https://doi.org/10.1016/j.tmaid.2024.102711.

Abstract :

The emergence of Highly Pathogenic Avian Influenza viruses (HPAIV), particularly H5 and H7 subtypes, continues to raise concerns regarding their potential to cause zoonotic pandemics. Since 2004, 874 cases of avian influenza A(H5N1) have been reported globally, with a high fatality rate. Following a period of silence, H5N1 reemerged in North America in 2021, subsequently spreading to South America via migratory birds. Colombia declared a health emergency in 2022, marking the onset of HPAIV outbreaks in the region. Between 2022 and early 2024, numerous outbreaks occurred, particularly affecting backyard birds, with significant ecological and economic implications. The role of migratory birds in disseminating HPAIV underscores the necessity for robust genomic surveillance and the One Health approach, integrating human, animal, and environmental health. Although person-to-person transmission has not been reported in South America, the virus's presence in mammals poses a risk for recombination and heightened pandemic potential. Continuous global monitoring and proactive vaccine development are essential to mitigate the risks associated with future respiratory virus outbreaks.

Keywords : *Preventive medicine public health; Highly pathogenic avian influenza virus; H5N1; Migratory bird; One health; Influenza A virus; Orthomyxovirus; Reemerging infectious diseases*

44. **Financial impacts of a housing order on commercial free range egg layers in response to highly pathogenic avian influenza,** Andrew P. Barnes, Nick Sparks, Irmelin S. Helgesen, Tarek Soliman, Preventive Veterinary Medicine, Volume 228, 2024, 106209, https://doi.org/10.1016/j.prevetmed.2024.106209.

Abstract:

Recent annual outbreaks of Highly Pathogenic Avian Influenza (HPAI) have led to mandatory housing orders on commercial free-range flocks. Indefinite periods of housing, after poultry have had access to range, could have production and financial consequences for free range egg producers. The impact of these housing orders on the performance of commercial flocks is seldom explored at a business level, predominantly due to the paucity of commercially sensitive data. The aim of this paper is to assess the financial and production impacts of a housing order on commercial free-range egg layers. We use a unique data set showing week by week performance of layers gathered from 9 UK based farms over the period 2020–2022. These data cover an average of 100,000 laying hens and include two imposed housing orders, in 2020/2021 and in 2021/22. We applied a random intercept linear regression to assess impacts on physical outputs and inputs, bird mortality and the impacts on revenue, feed costs and margin over feed cost. Feed use and feed costs per bird increased during the housing order which is a consequence of increased control over diet intake in housed compared to ranged birds. An increase in revenue was also found, ostensibly due to a higher proportion of large eggs produced, leading to a higher margin over feed cost. Overall, these large commercial poultry sheds were able to mitigate some of the potential adverse economic effects of housing orders. Potential negative impacts may occur dependant on the duration of the housing order and those farms with less control over their input costs.

Keywords: *Free Range Egg Layers; Highly Pathogenic Avian Influenza; Animal health economics; Multilevel Models*

45. **Genetic and biological properties of H9N2 avian influenza viruses isolated in central China from 2020 to 2022,** Libin Liang, Yaning Bai, Wenyan Huang, Pengfei Ren, Xing Li, Dou Wang, Yuhan Yang, Zhen Gao, Jiao Tang, Xingchen Wu, Shimin Gao, Yanna Guo, Mingming Hu, Zhiwei Wang, Zhongbing Wang, Haili Ma, Junping Li, Journal of Integrative Agriculture, Volume 23, Issue 8, 2024, Pages 2778-2791, https://doi.org/10.1016/j.jia.2024.03.055.

Abstract:

The H9N2 subtype of avian influenza virus (AIV) is widely prevalent in poultry and wild birds globally, and has become the predominant subtype circulating in poultry in China. The H9N2 AIV can directly or indirectly (by serving as a “donor virus”) infect humans, posing a significant threat to public health. Currently, there is a lack of in-depth research on the prevalence of H9N2 viruses in Shanxi Province, central China. In this study, we isolated 14 H9N2 AIVs from October 2020 to April 2022 in Shanxi Province, and genetic analysis revealed that these viruses belonged to 7 different genotypes. Our study on animals revealed that the H9N2 strains we identified displayed high transmission efficiency among chicken populations, and exhibited diverse replication abilities within these birds. These viruses could replicate efficiently in the lungs of mice, with one strain also demonstrating the capacity to reproduce in organs like the brain and kidneys. At the cellular level, the replication ability of different H9N2 strains was evaluated using plaque formation assays and multi-step growth curve assays, revealing significant differences in the replication and proliferation efficiency of the various H9N2 viruses at the cellular level. The antigenicity analysis suggested that these isolates could be classified into 2 separate antigenic clusters. Our research provides crucial data to help understand the prevalence and

biological characteristics of H9N2 AIVs in central China. It also highlights the necessity of enhancing the surveillance of H9N2 AIVs.

Keywords: *avian influenza virus; H9N2; central China; pathogenicity; antigenicity*

46. **Emerging threats: Is highly pathogenic avian influenza A(H5N1) in dairy herds a prelude to a new pandemic?,** Francesco Branda, Chiara Romano, Marta Giovanetti, Alessandra Ciccozzi, Massimo Ciccozzi, Fabio Scarpa, Travel Medicine and Infectious Disease, Volume 59, 2024, 102721, https://doi.org/10.1016/j.tmaid.2024.102721.

Abstract :

The recent detection of Highly Pathogenic Avian Influenza (HPAI) A(H5N1) in dairy cattle across several U.S. states has raised significant concerns about the virus's transmission dynamics and implications for public health. This unprecedented occurrence marks a divergence from typical avian hosts, potentially introduced by migratory birds. Symptoms in infected cattle, including decreased milk production, highlight the outbreak's severity. Although the CDC assesses the public health risk as low, heightened vigilance is warranted due to the risk of zoonotic transmission. Current measures include genomic surveillance and biosecurity protocols to curb spread. Genetic analyses reveal ongoing evolution in the virus, with sites under positive selection in mammalian hosts indicating possible adaptations that could increase transmissibility. A coordinated One Health approach is essential for effective monitoring and rapid response. While no spillover events have been confirmed, the potential for future transmission necessitates immediate and robust surveillance efforts to safeguard human, animal, and environmental health.

Keywords: *HPAI; A(H5N1); dairy cattle; zoonotic transmission; genomic surveillance; One Health; public health risk; biosecurity measures.*

47. **Protection conferred by an H5 DNA vaccine against highly pathogenic avian influenza in chickens: The effect of vaccination schedules,** Julie Valentin, Fiona Ingrao, Fabienne Rauw, Bénédicte Lambrecht, Preventive, safety and control measures against Avian Influenza A(H5N1)in occupationally exposed groups, Vaccine, Volume 42, Issue 7, 2024, Pages 1487-1497, https://doi.org/10.1016/j.vaccine.2023.11.058.

Abstract:

H5 highly pathogenic avian influenza (HPAI) viruses of the Asian lineage (A/goose/Guangdong/1/96) belonging to clade 2.3.4.4 have spread worldwide through wild bird migration in two major waves: in 2014/2015 (clade 2.3.4.4c), and since 2016 up to now (clade 2.3.4.4b). Due to the increasing risk of these H5 HPAI viruses to establish and persist in the wild bird population, implementing vaccination in certain sensitive areas could be a complementary measure to the disease control strategies already applied. In this study, the efficacy of a novel DNA vaccine, encoding a H5 gene (A/gyrfalcon/Washington/41088-6/2014 strain) of clade 2.3.4.4c was evaluated in specific pathogen-free (SPF) white leghorn chickens against a homologous and heterologous H5 HPAI viruses. A single vaccination at 2 weeks of age (1

dose), and a vaccination at 2 weeks of age, boosted at 4 weeks (2 doses), with or without adjuvant were characterized. The groups that received 1 dose with or without adjuvant as well as 2 doses with adjuvant demonstrated full clinical protection and a significant or complete reduction of viral shedding against homologous challenge at 6 and 25 weeks of age. The heterologous clade 2.3.4.4b challenge of 6-week-old chickens vaccinated with 2 doses with or without adjuvant showed similar results, indicating good cross-protection induced by the DNA vaccine. Long lasting humoral immunity was observed in vaccinated chickens up to 18 or 25 weeks of age, depending on the vaccination schedule. The analysis of viral transmission after homologous challenge showed that sentinels vaccinated with 2 doses with adjuvant were fully protected against mortality with no excretion detected. This study of H5 DNA vaccine efficacy confirmed the important role that this type of so-called third-generation vaccine could play in the fight against H5 HPAI viruses.

Keywords: *DNA vaccine; Avian influenza; Layers; Protective efficacy; Long lasting immunity*

48. **Clustering broiler farmers based on their behavioural differences towards biosecurity to prevent highly pathogenic avian influenza,** Hai-ni Pao, Elizabeth L. Jackson, Tsang-sung Yang, Jyan-syung Tsai, Yi-ting Hwang, Watson H.T. Sung, Dirk U. Pfeiffer, One Health, Volume 19, 2024,m100852, https://doi.org/10.1016/j.onehlt.2024.100852.

Abstract:

Highly pathogenic avian influenza (HPAI) is an important zoonotic disease. The study aims to identify farmer behaviour types to inform the design of behaviour change programmes for mitigating the transmission of HPAI. Therefore, the study utilised multivariate statistical analysis for gaining a better understanding of the relationships among farmers' 30 biosecurity behaviours, the risk of HPAI infection, and distinct features of commercial broiler farmers, which is different from using simple and few binary biosecurity measures. Convenience sampling was used to collect data from 303 Taiwan's farmers among which 40 farmers (13.2%) self-reported having had a HPAI outbreak in the study year while 16 farmers (5.3%) self-reported having had a HPAI outbreak in the past two years. Using categorical principal components analysis and a two-stage cluster analysis, four farmer clusters were identified with distinct features: 1)'Reserved' (4.6%) tended to choose 'No idea' for answering specific questions about HPAI; 2)'Secure' (76.3%) had a higher biosecurity status than the other farms; 3) 'Jeopardised' (16.8%) had a lower biosecurity status than the other farms; 4) 'No-response' (2.3%) tended to skip specific questions about HPAI. The biosecurity status of the 'Reserved' and 'No-response' clusters was undetermined, placing these farms at risk of HPAI infection. Compared to the 'Secure' cluster, the 'Jeopardised' cluster exhibited higher odds of self-reported HPAI in the study year (OR: 2.61, 95% CI: 1.22–5.58) and in the past two years (OR: 4.28, 95% CI: 1.39–13.19). Additionally, the 'Jeopardised' cluster showed increased odds of HPAI recurrence (OR: 4.01, 95% CI: 1.41–11.43). Our study demonstrates that inadequate biosecurity practices can elevate the occurrence or recurrence of HPAI outbreaks. The findings underscore the importance of distinguishing between these clusters to accurately assess the risk of HPAI infection across farms. Furthermore, understanding farmers' behaviours can inform the development of strategies aimed at behaviour change among farmers.

Keywords: *Avian influenza; biosecurity; Commercial broiler; Categorical principal components analysis; Cluster analysis*

49. **Survey of exposure to stranded dolphins in Japan to investigate an outbreak of suspected infection with highly pathogenic avian influenza (H5N1) clade 2.3.4.4(b) in humans,** Taishi Kayano, Tetsuro Kobayashi, Seiko Fujiwara, Yuta Okada, Hiroshi Nishiura, New Microbes and New Infections, Volume 56, 2024, 101214, https://doi.org/10.1016/j.nmni.2023.101214.

Abstract:

A highly pathogenic avian influenza (HPAI) A (H5N1) virus has been detected in domestic and wild animals worldwide. The incidence of HPAI infections in sea mammals has been increasing, as is the number of stranded marine mammals linked to H5N1 viral clade 2.3.4.4(b). In this study, we investigated a stranding event involving dolphins and human–dolphin contact, and investigated the potential risk of animal-to-human H5N1 transmission with a survey of exposure on the Tsurigasaki coast, Japan.

Methods

We performed a non-random, convenient-sample-based, survey on Tsurigasaki beach where around 30 melon-headed whales were stranded on April 3, 2023. Face-to-face (n = 25) and telephone (n = 1) interviews among surfers took place on April 7 and 8. A nasal swab for quick antigen testing was taken from those who wished to be tested (n = 13), to detect infections with influenza A virus.

Results

Although there was no confirmatory diagnosis of H5N1 in either humans or dolphins (while n = 3 dolphins were autopsied), we found that a large number of surfers had touched the dolphins with their bare hands while attempting to rescue them, and that some surfers were directly exposed to dolphin blood and body fluids in the ocean.

Conclusions

The adequate communication of risk is required to minimize the threat of viral transmission at this particular human–animal interface. Administrative and legal responses to cross-species transmission, including guidelines via one health frameworks, a rapid evaluation process of ethical approval, and the systematic involvement of experts in infectious disease, must be urgently formulated.

Keywords: *H5N1; Dolphin; Avian influenza; Cross-sectional survey; Risk communication*