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From avian to human: understanding the cross-species transmission and the global spread of highly pathogenic avian influenza

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Abstract

The global spread of avian influenza, particularly the highly pathogenic strains like H5N8 and H5N1, continues to pose significant challenges in terms of public health, animal health, and economic impact. Recent outbreaks have underscored the virulence and destructive capacity of these viruses, emphasizing the urgent need for effective surveillance, diagnosis, and control measures. This article explores the multifaceted nature of avian influenza outbreaks, from the clinical presentation in birds to the broader implications for human health. We discuss the crucial role of advanced diagnostic techniques, such as real-time reverse transcription polymerase chain reaction (RRT-PCR), which have been instrumental in identifying and subtyping the virus during outbreaks. Moreover, the potential for zoonotic transmission highlights the need for a One Health approach that integrates human, animal, and environmental health strategies to manage and prevent outbreaks. The challenges of vaccine development and deployment are also considered, particularly the need for vaccines that can keep pace with the rapidly mutating virus. Finally, the article advocates for global cooperation in research, surveillance, and response strategies to better predict, prevent, and respond to these outbreaks. This comprehensive perspective emphasizes the complexity of avian influenza as a global health issue and the multi-layered strategies required to combat it.

Keywords: *Avian influenza, H5N1, H5N8, epidemiology, zoonotic transmission, vaccine development, diagnostic challenges, global health.*

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Evidence in Context

- Article analyzes global impacts of H5N8 and H5N1 avian influenza on health and economy.
- Highlights the role of RT-PCR in managing avian influenza outbreaks.
- Advocates for a One Health approach to prevent and control outbreaks.
- Discusses the challenges of developing rapidly adaptable vaccines.
- Urges global collaboration in research and outbreak management.

To view Article

Introduction

The world has watched with increasing concern as various strains of avian influenza, most notably the highly pathogenic avian influenza virus A(H5N1) clade 2.3.4.4b, continue to spread globally [1,2]. First identified in domestic waterfowl in southern China in 1996, H5N1 has evolved significantly, affecting not only birds but also mammals, including humans. The recent detection of this virus strain in a diverse array of species, from minks and dolphins to seals and even polar bears, marks a troubling trend in the potential for cross-species transmission and raises urgent questions about our preparedness for a pandemic stemming from zoonotic diseases [3].

Highly Pathogenic Avian Influenza

The ongoing panzootic of highly pathogenic avian influenza (HPAI) A(H5N1) in wild birds and poultry poses an escalating zoonotic threat, as evidenced by the sporadic human infections reported globally since 2022 [3]. These human cases have been primarily associated with direct exposures to infected poultry, with a notable absence of human-to-human transmission. However, recent reports from the United States in 2024 indicate a concerning development: three dairy farm workers contracted HPAI A(H5N1) through exposure to infected dairy cattle, marking a rare instance of mammalian transmission [4]. Such cases highlight the virus's capacity for host diversity and underscore the complexity of controlling its spread across different species.

The rarity of HPAI A(H5N1) infections in humans can largely be attributed to the viral strains' inability to effectively bind to receptors predominating in the human upper respiratory tract [5]. This biological limitation has thus far played a crucial role in curtailing the broader spread among the human population and maintaining a relatively low public health risk from these viruses. However, the potential for viral evolution remains a significant concern. Influenza viruses are notorious for their rapid mutation rates and genetic reassortment capabilities, which could alter their pathogenicity and transmissibility. The global prevalence of HPAI A(H5N1) in birds and the recent spillovers into mammalian hosts necessitate vigilant monitoring and frequent reassessment of the virus's pandemic potential [6].

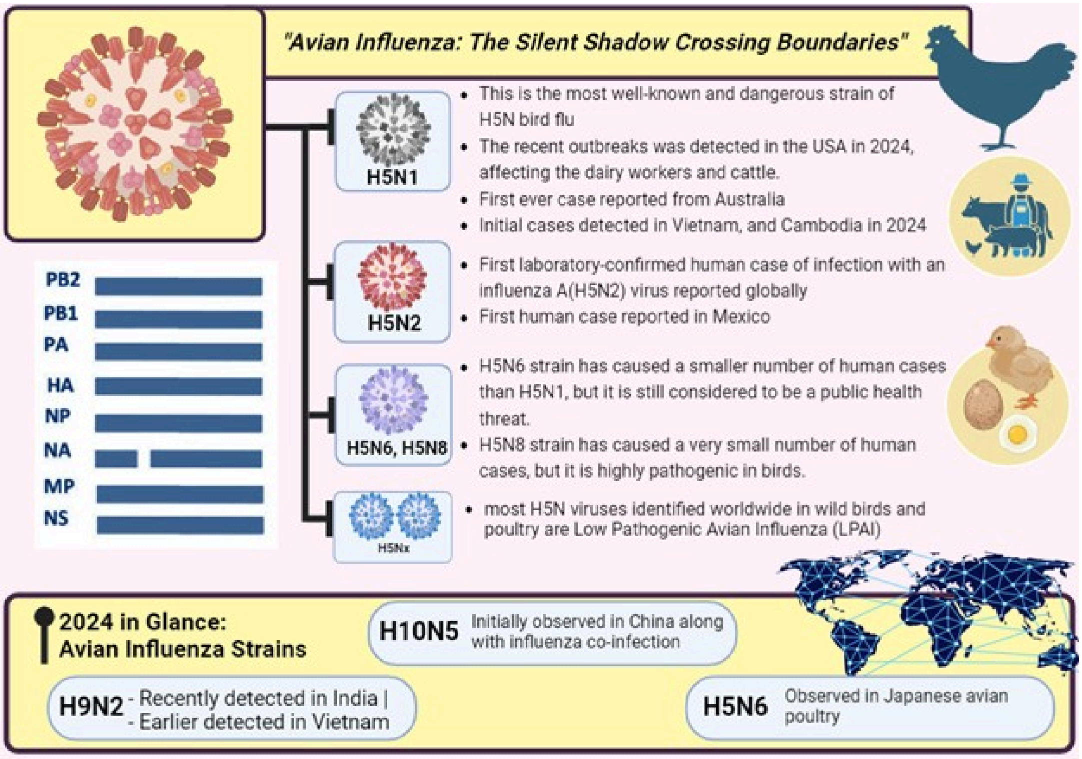

Figure 1: Overview of Avian Influenza Strains and Their Global Impact in 2024

Historical Context and Current Outbreaks

Since its first detection, H5N1 has been responsible for over 860 human infections with a case fatality rate exceeding 50% [7]. The virus's ability to diversify into multiple genetic clades and its spread across continents highlights its adaptability and persistence. Recent outbreaks in mammals, such as the 2022 incidents involving harbor and grey seals in New England, further complicate the epidemiological landscape. These events not only signify a broad host range but also suggest environmental transmission vectors that facilitate the virus's spread beyond traditional avian hosts.

Figure 1 highlights the H5N1 strain, known for its dangerous potential and recent outbreaks in the USA affecting dairy workers. Other strains like H5N2, H5N6, and H5N8 are also discussed, noting their varying degrees of pathogenicity and incidence rates in human infections. The figure includes visual representations of the virus, indicating different genetic components such as PB2, PB1, PA, HA, NP, NA, MP, and NS, providing insight into the structural complexity of these viruses. Additionally, it maps the detection of other strains like H9N2 and H10N5 across different

Countries, emphasizing the global prevalence and mutation potential of these viruses. This infographic serves as a comprehensive snapshot of the ongoing challenges posed by Avian Influenza in 2024, underscoring the need for continued vigilance and research.

Table 1: Summary of Highly Pathogenic Avian Influenza Outbreaks in 2024

Country of Origin	Influenza Strain (H#N#)	Species affected	Human Infections Reported
India	H9N2	Poultry and Wild birds	Yes (1 case)
Mexico	H5N2	Poultry	Yes (1 case)
Australia	H5N1	Poultry and Wild birds	Yes (1 case)
Vietnam	H5N1, H9N2	Poultry and Wild birds	H5N1 (1), H9N2 (1)
USA	H5N1	Dairy cattle and poultry	Yes (3 cases)
China	H10N5	Poultry and Wild birds	Yes, (1 case)
Cambodia	H5N1	Poultry and Wild birds	Yes (2 cases)

Viral Evolution

The viral evolution of highly pathogenic avian influenza (HPAI) is a complex and dynamic process driven by the virus's inherent capacity for rapid genetic changes. HPAI viruses, such as the H5N1 strain, undergo frequent mutations and genetic reassortments, which can significantly alter their virulence, host specificity, and transmission capabilities [8]. These changes often occur when different strains of the virus co-infect a host, leading to the exchange of genetic material—a process known as reassortment. Such genetic shifts and drifts enable HPAI viruses to adapt to new hosts and environmental conditions, increasing their potential to cause widespread outbreaks across diverse species barriers. This constant evolution poses significant challenges for disease surveillance and control, necessitating continuous monitoring and adjustment of strategies to mitigate the threat posed by these ever-changing viral pathogens [2,9].

Table 2: Key Genetic Mutations Associated with Cross-Species Transmission

Gene	Mutation	Effect on Transmission	Notable Strains
HA	Q226L	Increased binding to mammalian receptors	H5N1 clade 2.3.4.4b
PB2	E627K	Enhanced replication in mammalian cells	H5N1, H7N9
HA	N182K	Altered receptor binding specificity	H5N1
PB2	D701N	Improved polymerase activity	H7N9

Mechanisms of Cross-Species Transmission

The mechanisms underlying cross-species transmission of avian influenza are complex and multifaceted. Genetic mutations, particularly in the hemagglutinin (HA) and polymerase basic 2 (PB2) genes, appear to enhance the virus's ability to infect mammals [10]. These genetic shifts could potentially increase the virus's affinity for receptors found in the upper respiratory tracts of humans and other mammals, although such changes have not yet been observed in the current strains circulating globally.

Zoonotic Potential and Human Health Risks

While the direct transmission of H5N1 from birds to humans remains rare, the sporadic cases that do occur are alarmingly lethal. The possibility of the virus adapting to facilitate easier human-to-human transmission could herald a public health catastrophe comparable to or exceeding the scale of the COVID-19 pandemic. Global health organizations remain vigilant, monitoring genetic changes in the virus that could indicate an increased risk to humans [6].

Table 3: Pathogenicity of various strains of Avian Influenza

Strain	Pathogenicity	Host Range	Human Infection Cases	Case Fatality Rate	Year of Emergence	Notable Outbreaks
H5N1	High	Birds, Mammals	Over 860	~40%	1997	Asia, Africa, Europe
H5N8	High	Birds	Rare	Low	2014	Europe, Asia, Africa
H7N9	Low to High	Birds	Over 1500	~33%	2013	China
H9N2	Low	Birds	Sporadic	Low	1999	Asia, Middle-East

Implications for Global Health Surveillance and Response

The ongoing evolution of H5N1 necessitates a robust global surveillance system, capable of detecting and responding to outbreaks in both wildlife and domestic animals, particularly cattle, dairy, and poultry [4]. The development of vaccines against specific clades of the virus is crucial, yet challenging, given the rapid antigenic changes observed in H5N1. Effective pandemic preparedness strategies must incorporate not only technological advancements in vaccine development and diagnostics but also policies that minimize human exposure to potential zoonotic vectors [11].

Diagnostic Challenges and the Role of Advanced Technologies

One of the primary challenges in managing avian influenza outbreaks is the timely and accurate diagnosis of the virus strains involved. In the Algerian outbreaks [12], the use of real-time reverse transcription polymerase chain reaction (RRT-PCR) was pivotal in identifying and subtyping the H5N8 and H5N1 strains. This technology, along with specific PCR for hemagglutinin (HA) and neuraminidase (NA) identification, provided crucial data for outbreak management. However, the effectiveness of these diagnostic tools depends heavily on the availability of resources and the speed at which samples can be processed, which poses significant challenges in resource-limited settings.

Table 4: Comparison of Diagnostic Techniques

Diagnostic Method	Accuracy	Time to Results	Cost (relative)	Advantages	Limitations
RRT-PCR	High	4-6 hours	High	High sensitivity, specific	Requires lab setup, potential false positives/negatives
Rapid Antigen Test	Medium	15-30 minutes	Low	Quick results	Lower sensitivity, may require confirmation with other tests
Virus Isolation	High	5-10 days	High	Definitive identification	Time consuming, requires specialized facilities
Serological Tests	Medium	1-2 days	Medium	Detects past infections	Cannot detect active infection

Transmission Dynamics and Zoonotic Potential

The epidemiological investigation of avian influenza is complicated by the virus's ability to spread rapidly among flocks and its potential to mutate and cross species barriers. The transmission of avian influenza from poultry to humans remains a significant concern, as highlighted by historical epidemics and the ongoing need for vigilance [9]. Understanding the

Transmission dynamics, including the role of migratory birds in spreading the virus across borders is critical for developing targeted control measures.

Public Health Implications and Response Strategies

The threat of avian influenza to public health cannot be overstated, particularly considering the potential for the virus to gain human-to-human transmissibility. The outbreaks in Algeria have highlighted the need for robust surveillance systems that integrate human and animal health

Data, facilitating early detection and swift response to potential zoonotic spillover [12]. Public health responses must be proactive, focusing on both containment measures at the source and the protection of human populations [13].

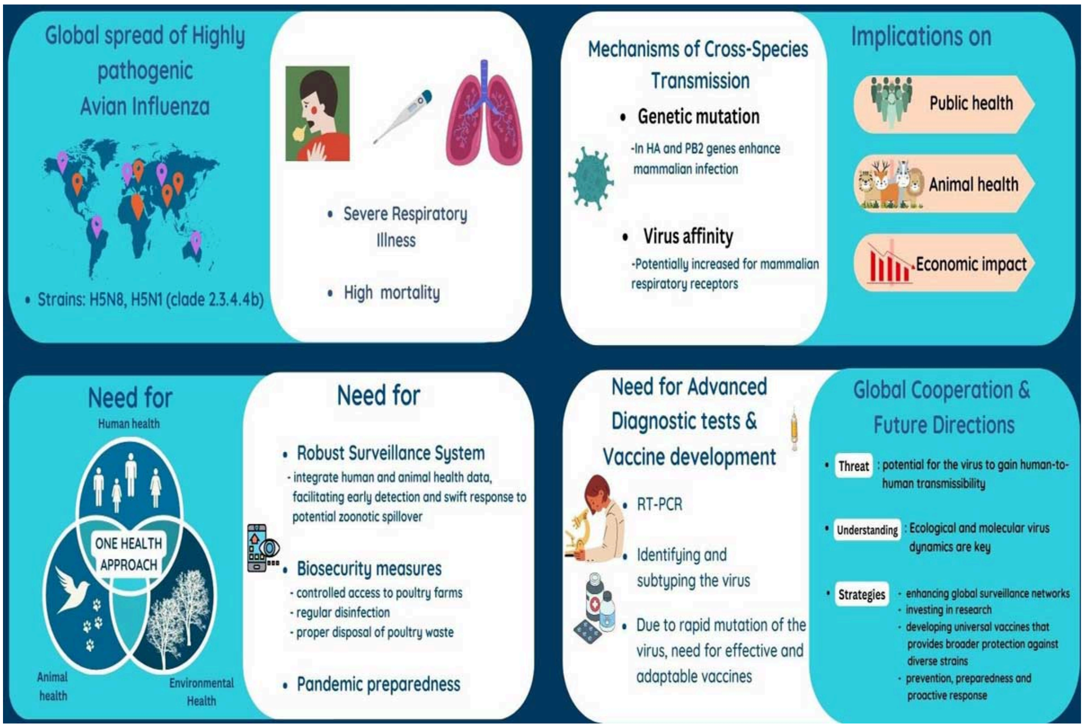

Figure 4 illustrating global spread of Avian Flu and underscoring the public health, animal health, one health approach are essential for managing avian influenza.

Prevention and Control: Biosecurity and Vaccination

Effective control and prevention strategies are essential in curbing the spread of avian influenza. Biosecurity measures, including controlled access to poultry farms, regular disinfection, and the proper disposal of poultry waste, are fundamental components of preventing outbreak escalation. Additionally, vaccination programs for poultry can significantly reduce the incidence of the disease. However, the development of vaccines must keep pace with the evolving nature of the virus, ensuring efficacy against current strains [14].

Global Cooperation and Future Directions

The fight against avian influenza is not confined to individual countries; it requires a coordinated global effort. International cooperation in sharing epidemiological data, research on virus transmission, and vaccine development is crucial. Future strategies should focus on enhancing global surveillance networks, investing in research to understand the mechanisms of virus mutation and adaptation, and developing universal vaccines that can provide broader protection against diverse influenza strains [8].

Conclusion

The cross-species transmission of avian influenza, particularly of the H5N1 clade 2.3.4.4b, presents a clear and present danger to global health. Understanding the ecological and molecular dynamics of this virus is essential for developing strategies to mitigate its impact. As the world grapples with the fallout from the COVID-19 pandemic, the lessons learned must inform our approach to emerging infectious diseases, emphasizing prevention, preparedness, and prompt response to potential zoonotic threats.

Supporting information

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Ethical Considerations

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References

1. Uyeki TM, Milton S, Abdul Hamid C, Reinoso Webb C, Presley SM, Shetty V, et al. Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker. N Engl J Med. *2024;390(21):2028-9 [Crossref][PubMed][Google Scholar]*

2. Pulit-Penaloza JA, Brock N, Belser JA, Sun X, Pappas C, Kieran TJ, et al. Highly pathogenic avian influenza A(H5N1) virus of clade 2. 3. *4.4b isolated from a human case in Chile causes fatal disease and transmits between co-housed ferrets. Emerg Microbes Infect. 2024;13(1):2332667 [Crossref][PubMed][Google Scholar]*

3. Huang P, Sun L, Li J, Wu Q, Rezaei N, Jiang S, et al. Potential cross-species transmission of highly pathogenic avian influenza H5 subtype (HPAI H5) viruses to humans calls for the development of H5-specific and universal influenza vaccines. Cell Discov. *2023;9(1) [Crossref][PubMed][Google Scholar]*

4. Abbasi J. As a Third Worker Tests Positive for Bird Flu in US Dairy Cattle Outbreak, Here's What to Know. JAMA. *2024 [Crossref][PubMed][Google Scholar]*

5. Al-Tawfiq JA, Tirupathi R, Temsah M-H. Feathered fears: Could avian H5N1 influenza be the next pandemic threat of disease X? New Microbes New Infect. 2024;59. *[Crossref][PubMed][Google Scholar]*

6. The Lancet Infectious D. What is the pandemic potential of avian influenza A(H5N1)? Lancet Infect Dis. 2024;24(5). *[Crossref][PubMed][Google Scholar]*

7. Garg S, Reed C, Davis CT, Uyeki TM, Behravesh CB, Kniss K, et al. Outbreak of Highly Pathogenic Avian Influenza A(H5N1) Viruses in U. S. *Dairy Cattle and Detection of Two Human Cases - United States, 2024. MMWR Morb Mortal Wkly Rep. 2024;73(21):501-5 [Crossref][PubMed][Google Scholar]*

8. Bruno A, de Mora D, Olmedo M, Garces J, Alfaro-Nunez A, Garcia-Bereguiain MA. Evolutionary history of human infections with highly pathogenic H5 avian influenza A virus: a new front-line global health threat established in South America. J Travel Med. *2023;30(7) [Crossref][PubMed][Google Scholar]*

9. Sun H, Li H, Tong Q, Han Q, Liu J, Yu H, et al. Airborne transmission of human-isolated avian H3N8 influenza virus between ferrets. Cell. *2023;186(19):4074-84 e11 [Crossref][PubMed][Google Scholar]*

10. Stanislawek WL, Tana T, Rawdon TG, Cork SC, Chen K, Fatoyinbo H, et al. Avian influenza viruses in New Zealand wild birds, with an emphasis on subtypes H5 and H7: Their distinctive epidemiology and genomic properties. PLoS One. *2024;19(6):e0303756 [Crossref][PubMed][Google Scholar]*

11. Giacinti JA, Robinson SJ, Sharp CM, Provencher JF, Pearl DL, Stevens B, et al. Assessing avian influenza surveillance intensity in wild birds using a One Health lens. One Health. *2024;18:100760 [Crossref][PubMed][Google Scholar]*

12. Ammali N, Kara R, Guetarni D, Chebloune Y. Highly pathogenic avian influenza H5N8 and H5N1 outbreaks in Algerian avian livestock production. Comp Immunol Microbiol Infect Dis. *2024;111:102202 [Crossref][PubMed][Google Scholar]*

13. Ebrahim SH, Zumla A, Wong J, Ur Rahman M, Al-Abri SS, Al Rabeeah AA, et al. Reducing the risk of highly pathogenic avian influenza A virus H5N1 transmission during the Hajj. Nat Med. *2024 [Crossref][PubMed][Google Scholar]*

14. Golgol E, Mayahi M, Boroomand Z, Shoshtari A. Effect of Vaccination on Distribution and Immune Response of Avian Influenza Virus H9N2 in Coturnix coturnix. Arch Razi Inst. *2023;78(6):1746-52 [Crossref][PubMed][Google Scholar]*

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