Bird Flu: Science vs. Silence: Part 1

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Global infectious disease incidents in the 20th and 21st centuries have involved multiple types of respiratory viruses. While the human toll from the COVID-19 pandemic, caused by an airborne coronavirus (SARS-CoV-2), is still being calculated, influenza viruses remain the most common microorganisms responsible for sporadic widespread human epidemics and pandemics. The most dramatic example of this was a novel A(H1N1) influenza virus responsible for the global 1918–1919 “Spanish Influenza” pandemic. Between 30-50 million people died in a little over one year. Fast-forward to the present, and the current strain of pathogenic A(H5N1) avian influenza virus is considered by many scientists to constitute a major emerging respiratory viral threat.

The first avian influenza human cases attributed to the A(H5N1) virus were reported in Hong Kong in 1997, with isolation of this strain from 18 infected people, six of whom died from the illness. This human outbreak coincided with a massive epidemic of highly pathogenic avian influenza in the region’s domestic poultry population. Widespread alarm was rapidly followed by emergency destruction of the entire poultry population of Hong Kong, approximately 1.5 million birds. This drastic, yet necessary, response was credited with delaying the progression of H5N1 in Southeast Asia, as subsequent infections in poultry and humans in the region did not appear again until 2003. In 2003 and early 2004, however, new outbreaks among poultry in eight Asian countries signaled a precursor of the human infections to follow. Even with the destruction of hundreds of millions of birds in affected countries, relief from the avian pandemic was only temporary. From 2003 to 2024, more than 900 confirmed human cases of A(H5N1) were reported across 24 countries, with a very high fatality rate. The virus spread to North America in 2021, and it reached Central and South America by 2022, primarily through wild migratory birds. According to the WHO and CDC, as of January 2025, there have been 964 confirmed human cases of A(H5N1), with ongoing reports of infections in poultry and wild birds across many countries. The lethality of this strain is stark compared with seasonal influenza outbreaks, with more than 48% (466) of those diagnosed with the disease have died.

The following two-part series will consider major issues surrounding microbiological, epidemiological, and clinical challenges presented by avian Type A influenza viruses. Our focus will be on the current A(H5N1) bird flu challenge, and the discussion will be framed by primarily using a question-answer format. Features differentiating avian influenza (i.e., “bird flu”) from seasonal human influenza outbreaks will be highlighted, along with a discussion of the evolving nature of viral transmission and the potential for a widespread outbreak. The second installment will include sections dealing with current and emerging zoonotic transmission threats for infections in humans, poultry, cows, and other mammalian species. Public health detection and prevention strategies will also be considered in light of ongoing developments involving cross-species viral transmission in birds, dairy cattle, and other animals.

Q: How are influenza viruses characterized, and what viral type is responsible for the most severe infections?

A: Influenza viruses are enveloped RNA Orthomyxoviruses that can cause moderate-to-severe upper and lower respiratory tract infections. These viruses are divided into three groups, designated Type A, Type B, and Type C. Influenza Type A viruses are the most common clinical isolates. They cause the most severe infections and are etiologies of most human epidemics. They are also the only influenza type that has caused widespread outbreaks (e.g., pandemics). These pathogenic viruses are subdivided by two surface protein differences: 1. hemagglutinin (HA), which is essential for viral attachment on respiratory tissue receptors, and 2. neuraminidase (NA), which facilitates viral release from infected cells **(Figure 1)**. At least 16 antigenically distinct HA subtypes (H1 to H16) and nine different NA (N1 to N9) subtypes have been described in influenza A viruses.

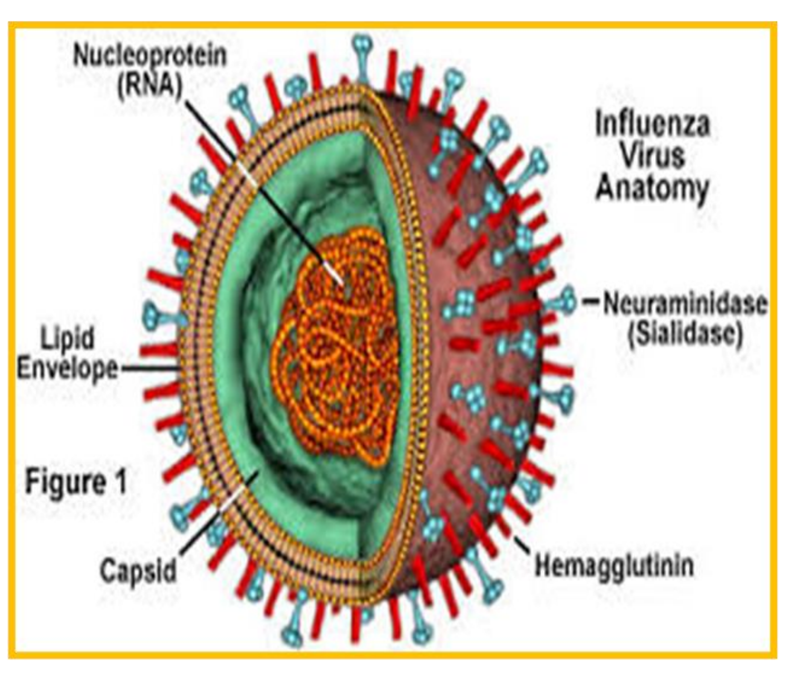

Figure 1: Structure of Influenza Viruses

Influenza Type B viruses also cause epidemic disease, but clinical illnesses tend to be milder than those caused by influenza A viruses. Although they have a similar structure as Type A viruses, they do not exhibit the same type of antigenic HA and NA variation, and thus, their classification does not include subtypes. Instead, they are classified into two distinct lineages: B/Victoria and B/Yamagata, which were named after their first virus representatives, B/Victoria/2/87 and /Yamagata/16/88, respectively.

In contrast, Influenza Type C viruses have not been associated with flu epidemics **(Figure 2)**.

With regard to infection control in healthcare settings, it is important to note here that the presence of an outer surface lipid envelope makes influenza viruses susceptible to many types of antivirals and disinfectants.

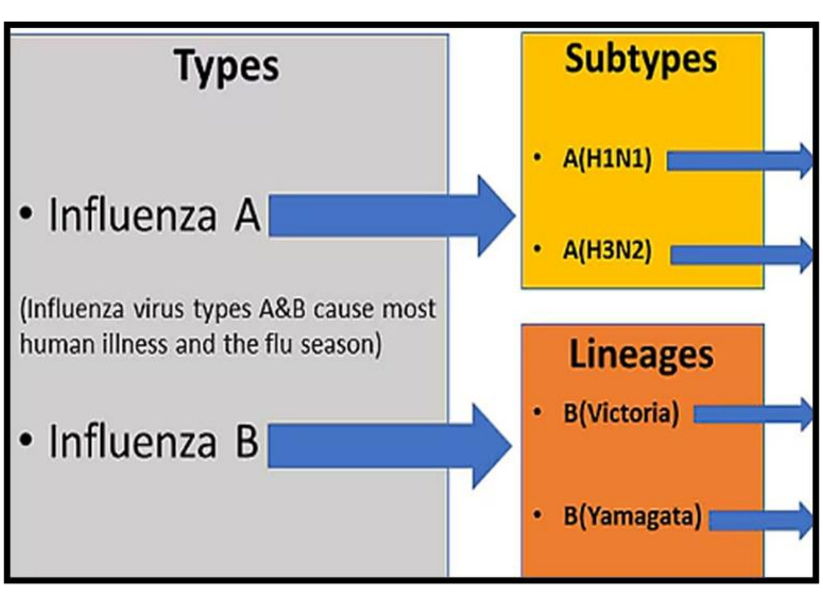

Figure 2. Examples of Influenza Virus Classification

Q: What do the abbreviations LPAI and HPAI signify when discussing bird flu?

A: Avian influenza A viruses are classified into two categories: *low pathogenic avian influenza* **(LPAI)** A viruses, and the earlier-noted *highly pathogenic avian influenza* **(HPAI)** A viruses. LPAI viruses cause either no signs of disease or mild disease in chickens/poultry, such as ruffled feathers and a drop in egg production. Most avian influenza A viruses are low-pathogenic and cause few signs of disease in infected wild birds. However, in poultry, some low-pathogenic viruses can mutate into HPAI viruses. These HPAI viruses cause severe disease and high mortality in infected poultry (**Table 1**). Only some avian influenza A(H5) and A(H7) viruses are classified as HPAI Type A viruses, while most A(H5) and A(H7) viruses circulating among birds are LPAI Type A viruses. HPAI A influenza virus infections can cause disease that affects multiple internal organs with a mortality of 90%-100% in chickens, often within 48 hours. Both LPAI and HPAI A viruses have also been demonstrated to cause mild-to-severe illness in infected humans. There are genetic and antigenic differences between the influenza A virus subtypes that typically infect only birds and those that can infect birds and people.

Based on Genetic Features and/or Disease Severity in Poultry

A. **Low Pathogenic Avian Influenza (LPAI)**
- H1 to H5 subtypes
- Mild illness: ruffled feathers; reduced egg numbers

B. **Highly Pathogenic Avian Influenza (HPAI)**
- LPAI H5 of H7 subtypes can mutate to HPAI
- Extremely contagious, rapidly fatal in birds
- ~100% mortality
- Birds can die same day as symptoms appear

Table 1. Brief Comparison of LPAI and HPAI in Poultry

Q: How capable are Type A influenza viruses at genetic modification to form new strains?

A: Influenza A viruses are perpetuated in wild birds, with these hosts functioning as natural reservoirs for specific avian strains. Unlike other susceptible birds, such as chickens, turkeys, and domestic ducks, wild ducks did not become ill from carriage of the virus in the intestines. However, in recent months, wild ducks have been experiencing high mortality rates, as evidenced by reports of hundreds of bird die-offs — especially along Lake Michigan and in areas like Michigan’s Lower Peninsula — from A(H5N1) influenza viruses.

What is especially pertinent to the emergence and spread of avian influenza is the genetic diversity demonstrated by influenza A viruses. New strains of influenza A viruses can be routinely generated either through viral mutation or reassortment of a virus’s genome with RNA segments from other animal species. The virus’s ability to rapidly mutate also provides opportunities for genetic reassortment between animal species. Resultant genetic modifications allow viruses to infect and spread to many animal species, such as domestic poultry, cows, pigs, cats, and multiple other mammalian species, including humans. One of the most remarkable earlier discoveries was the frequency with which influenza virus mutations can occur. Alteration of the viral antigen structure can lead to human infections with variants where little or no resistance is present in populations at risk. The former can be occasionally severe, with high hospitalization rates and deaths from secondary pneumonia.

Q: What is avian influenza, and how does it differ from seasonal and other pandemic influenza outbreaks?

A: It is helpful to begin with a few basic definitions to distinguish between these terms. *Seasonal influenza* is a contagious respiratory disease caused by multiple Type A and B influenza viruses. In contrast, *pandemic influenza* is a widespread, often global outbreak that occurs when a new influenza Type A virus subtype causes serious human disease and is easily transmitted from person to person. These new subtypes have usually never previously circulated through the human population. Viral subtypes that have not circulated among people for many decades can also trigger a pandemic. *Avian influenza,* commonly referred to as “bird flu,” is a contagious disease of animals caused by influenza viruses that normally infect only birds. A summary of avian influenza viruses is presented in **Table 2**. Many of the avian strains are highly contagious, with infected birds shedding viruses in feces, saliva, and nasal secretions. They are spread to other susceptible bird and animal hosts, including pigs and humans, primarily via fecal droppings and airborne particles that can contaminate inanimate surfaces or other environments. Airborne transmission can also occur from bird to bird as well as from bird to other animal hosts from viruses present in nasal and oral secretions. It should therefore become clear when this information is evaluated that at the present time, influenza is not considered an eradicable disease. Surveillance, prevention, and infection control strategies are the only realistic public health goals.

- All influenza viruses originate in birds, with most staying there.
- Wild migratory birds are natural viral hosts.
- Avian influenza strains far outnumber human strains.
- Normally, an influenza strain that infects birds does not attack humans, because it is unable to infect and grow in human cells.
- Some Type A avian influenza strains can adapt and mutate to where they infect other species, including people.
- Occasionally, a strain that infected only birds will cross species relatively intact to cause widespread human infections.

Table 2: Avian Influenza Viruses

Comparison of Seasonal Influenza With Avian A(H5N1) Influenza

In addition to describing viral virulence features and transmission between multiple animal species, ongoing investigation of influenza viruses since 1933 has led to the realization that these RNA viruses have been responsible for periodic epidemics and pandemics for hundreds of years. Influenza viruses are primarily transmitted via microbial-laden secretions in respiratory droplets. A sudden onset of constitutional and respiratory symptoms occurs after an incubation interval of usually 2 days (but can be 1–5 days), which typically are far more severe than those presenting with a cold. The most common influenza symptoms include a rapidly developing fever (100°–104° F), cough, sore throat, and muscle aches. In contrast, illness following infection with A(H5N1) influenza virus can present with a wide range of symptoms, ranging from those found with seasonal influenza to severe respiratory disease (e.g., pneumonia). Such secondary sequela can rapidly develop into life-threatening respiratory complications as worst-case scenarios. Following recovery from seasonal influenza, protection from reinfection is primarily associated with the development of antibodies to the HA antigen, but antibodies against NA are also protective. This antibody response is specific for each strain of virus; however, cell-mediated immunity is more general and capable of reacting to another influenza strain of the same type (influenza A or B virus).

In contrast to seasonal influenza, A(H5N1) bird flu is currently considered to be an uncommon but potentially serious infection in humans. Infections have been acquired through contact with infected animals like poultry or dairy cows, and they can cause symptoms ranging from mild to severe, with a high mortality rate. A brief summary of the current status of H5N1 bird flu infections in the United States follows:

Symptoms: Symptoms can range from mild flu-like symptoms (fever, cough, sore throat, fatigue) to severe illness (like pneumonia, respiratory distress, and multi-organ failure).

- Common symptoms:
  - Fever or feeling feverish
  - Cough, sore throat, runny or stuffy nose
  - Muscle or body aches, headaches, fatigue
  - Shortness of breath or difficulty breathing
  - Eye redness (conjunctivitis)
  - Less common symptoms: diarrhea, nausea, vomiting, or seizures
- Severe symptoms:
  - Pneumonia
  - Respiratory distress
  - Multi-organ failure

Transmission: H5N1 is primarily transmitted from infected animals (poultry, dairy cows, and other mammals) to humans. This occurs through contact with infected animals or contaminated surfaces; by inhaling respiratory droplets; or touching the eyes, nose, or mouth with contaminated hands. Infections have been documented in poultry workers, dairy workers, and, in one case, a person with no known exposure. There is no current evidence of sustained human-to-human transmission.

At-risk populations: People who work with animals, especially poultry or dairy cows, are at a higher risk of infection.

Current U.S. Situation (as of March 17, 2025):

- **Outbreak in Dairy Cows:** The current outbreak began in late March 2024 with the detection of H5N1 bird flu in dairy cows.
- **Human Cases:** Since April 2024, the Centers for Disease Control and Prevention (CDC) has confirmed bird flu in 70 people in the United States, with no evidence of human-to-human transmission.
- **Public Risk:** The CDC continues to assess that the current H5N1 bird flu risk to the general public remains low.
- **First U.S. Death:** In January 2025, a backyard chicken owner in Louisiana died after being infected, likely due to exposure to his backyard flock and wild birds, plus other health conditions that made him more vulnerable.

The Part 2 article to follow will provide additional detail into the modes of transmission and scope of A(H5N1) disease in humans and other susceptible species. Ongoing public health detection and prevention strategies will also be considered.

For the full list of references, CLICK HERE

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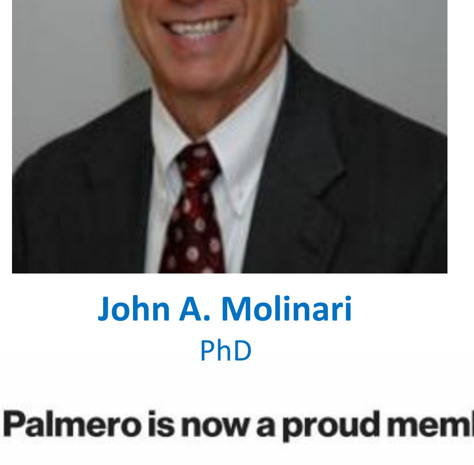

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