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Review Article

# An extensive review of current knowledge regarding avian influenza and its effects on human health.

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## Abstract

It is now widely recognised that avian influenza viruses are a hazard to public health, agricultural biosecurity, and may even be the source of pandemic human influenza viruses. There have been reports of human infections from Asia (H5N1, H5N2, H9N2), Africa (H5N1, H10N7), Europe (H7N7, H7N3, H7N2), and North America (H7N3, H7N2, H11N9) with the avian influenza A virus (subtype H5N1). This paper's goal is to evaluate what is currently known about avian influenza and its effects on public health. Low pathogenic and high pathogenic strains of the many avian influenza virus subtypes, such as H1N1, H7N2, H7N3, H7N7, and H9N2, can have an influence on public health. The extremely dangerous H5N1 "bird flu" virus is not the only source of these threats. Poultry is the main species affected by the disease's occurrences and outbreaks.

Economic losses resulting from avian influenza comprise depopulation and disposal expenses, significant morbidity and mortality losses, expenditures associated with quarantine and monitoring, and compensation for bird removal. Worldwide public health concerns have been raised by avian influenza because it poses a hazard to poultry, particularly hens. It has also demonstrated the ability to spread from chickens to people, where it can result in fatal infections. Several molecular and serological methods have made it much easier to diagnose human cases of avian flu. To prevent bird flu outbreaks, adherence to WHO guidelines for surveillance, public awareness, and pandemic preparedness is crucial. The implementation of management practices, such as personal hygiene, cleaning and disinfection techniques, and biosecurity principles, can effectively control the spread of avian influenza viruses. along with guidelines for processing and cooking. The emergence of extremely lethal avian influenza viruses as well as the recent zoonotic spread of the avian H5 and H7 viruses into humans are also described. The potential of a novel avian influenza virus causing a pandemic of humans still exists, despite the fact that prevention in domestic avian populations can reduce the risk to human health.

**Keywords :** *Avian Influenza virus; Bird flu; Outbreak; Poultry; Public health; Review*

## INTRODUCTION

Influenza virus A, a member of the family Orthomyxoviridae, is the virus that causes avian influenza (AI) or asymptomatic infection. Its genome is made up of eight segments of single-stranded negative-sense RNA [1]. The influenza virus is classified into four primary species: A, B, C, and D. Type A viruses are known to infect a large variety of birds and mammals, although the host ranges of other species are more restricted. All avian influenza viruses, including influenza A viruses (IAV), have eight distinct genomic regions that range in size from 890 to 2341 nucleotides [2]. One of the most dangerous viruses that endangers the health of humans and animals is the influenza A virus (IAV) [3]. Their potential to spread from one species to another and result in many viral genome reassortments is a serious health hazard. Ultimately, the four most well researched pandemic IVs—1918, 1957, 1968, and 2009—obtained all or a portion of their gene segments from the avian IAV gene pool, which contains second-order swine genes [4]. Over the past 20 years, there has been an increase in the number of avian influenza viruses (AIVs) that can cause serious illness in humans, and the role of pigs in the interspecies spread of IAVs remains concerning [5]. Avian influenza viruses are classified according to their genetic lineages, clades, subtypes, and pathotypes. Subtypes of avian influenza viruses exist. by the hemagglutinin (HA) and neuraminidase (NA) glycoproteins on their surface, which are important factors in determining the pathogenicity, transmission, and species-specific adaptation of the AI virus; nevertheless, these characteristics, along with infectivity, are multigenic. Nonetheless, the HA is the primary factor that determines pathogenicity. While neuraminidase's job is to release newly produced viruses, the HA is necessary for attachment and entry into cells for virus replication [1]. There are nine distinct neuraminidase (N1-9) subtypes and sixteen distinct hemagglutinin (H1-16) subtypes. These viruses have been found to be present in over 100 species of wild birds, primarily in the orders Anseriformes (ducks, geese, and swans) and Charadriiormes (gulls, terns). Nevertheless, they are usually not clinically pathogenic and are hence of low pathogenicity (LP) [6].

## Literature Review

### Etiology

Avian influenza is the source of the pandemic influenza virus [15]. Negative strand RNAs with eight segments make up its genetic material. Looking at the influenza A virus under an electron microscope reveals exterior spikes. Hemagglutinin (HA) spikes are approximately five times more frequent than neuraminidase (NA) spikes [16]. With the existence of 18 distinct hemagglutinin (HA) subtypes and 11 distinct neuraminidase (NA) subtypes, a total of 198 distinct viral strains are possible. There are only 131 subtypes known to exist in nature as of 2019 [1]. Several species are infected by influenza type A viruses. Humans can contract influenza types B and C, but pigs can also contract type C. The influenza strains that affect humans are always type A, whereas some are type B in birds. Even though not all of their strains can cause clinical illness, they are regarded as the most virulent category. The HA and NA surface proteins are used to categorise type A influenza viruses into subtypes. Generally speaking, there is little to no cross-protection across various HA or NA categories. The surface of virus type A has two significant proteins: HA: Adheres the virus to receptors on cells. NA: Allows the virus to spread to more cells. The classification of influenza viruses, such as Influenza A Beijing H1N1 or Influenza A Panama H3N2, is based on these proteins. These proteins are constantly changing. Because type A influenza viruses can cause extremely serious illness in birds, they are classified as highly pathogenic avian influenza (HPAI) or weakly pathogenic avian influenza (LPAI).

Young chickens were injected intravenously in the lab or by having specific genetic traits linked to HPAI viruses. Type A and essentially two subtypes of the H5 and H7 viruses, of which there are several strains that are more or less dangerous, are the viruses that cause avian influenza. The two varieties of glycoproteic spicules distinguish the strains from one another [17].

### Epidemiology

In Guangdong Province, China, the first H9N2 (LPAIV) and H5N1 (HPAIV) viruses were discovered in 1994 and 1996, respectively [18]. The avian flu epidemic was initially reported in Italy in 1878. Subsequently, the United States reported two significant epidemics of poultry in 1924 and 1929 [19]. Since the influenza virus caused the first recorded human case and death in Hong Kong in 1997, both domestic and wild birds have been known to contract the disease. Reports of HPAI H5N1 alone come from more than 77 nations [20]. Since 2003, 860 human cases have been reported; of those, more than 50% have resulted in H5N1-related deaths [21]. 1,568 human instances and 616 cases of Global reports of fatalities linked to the new H7N9 virus were made. Geographically, there have been more outbreaks in China, Vietnam, India, Taiwan, Israel, Japan, and South Korea than anywhere else in the world. The disease is most prevalent in Asia [22].

Geographic Distribution: The first reports of avian influenza viruses (AIVs) date back to 1878 [23]. 1934 saw the isolation of AI from hens in Italy [24]. The possible route of introduction for 36 of the 52 virus strains was identified by an integrated analysis that combined phylogenetic data with worldwide information on the trade in exotic birds, poultry imports, and bird migrations. Both poultry and migratory birds were traded in Asia and Africa as a result of spread, but in Europe, migratory birds predominated (20 out of 23 countries). It was believed that the spread of birds between North and South America was correlated with the importation of diseased chickens into North America [25].

### Transmission

Human influenza is transmitted by breathing virus droplets and nuclei, direct contact, indirect contact (fomite), and self-inoculation onto the mucosa of the upper respiratory tract or conjunctiva [27]. It has been reported that the avian influenza viruses H5N1 and H7N7 can spread from person to person. The H5N1 HPAI virus was first detected in humans during the 1997 pandemic in Hong Kong. Since then, reports of possible H5N1 viral transmission from humans to humans have come from Thailand, Vietnam, Indonesia, and Pakistan. Alongside an extensive sequence of outbreaks of the highly deadly H7N7 virus in Dutch poultry farms between Human-to-human transmission of the H7N7 virus was documented between March and May 2003, when at least one human fatality was linked to the virus out of the 89 cases confirmed at the time of the outbreak [28]. The virus that causes avian influenza is present in many different hosts. Water birds that fly freely, such as geese, ducks, shorebirds, and gulls, are important sources of AIVs.

**Clinical Signs**

The clinical signs of AI are greatly influenced by the virulence of the viruses implicated, the species affected, age, any concomitant bacterial or viral diseases, and the environment. The infections in poultry, particularly domestic ducks, may not show any symptoms and can only be detected by a serological test. Reduced feed consumption, cyanosis of the combs, wattles, and shanks, emaciation, increased broodiness of hens and decreased egg production, oedema of the head and face, diarrhoea, ruffled feathers, mild to severe respiratory signs, such as coughing, sneezing, rales, and excessive lacrimation, nervous disorder, and cyanosis of unfathered skin are all symptoms associated with HPAI viruses. Before any clinical signs appear, the bodies of some birds are found. Neurological symptoms and a decrease in typical vocalisations are possible [33]. For the most severely injured birds, the mortality rate could range from 50% to 100% [7]. The symptoms and indications may vary depending on the kind of avian influenza. The sickness was caused by a virus. Human infections caused by the LPAI virus are generally associated with moderate, non-fatal illnesses. Human LPAI A virus infections have been linked to conjunctivitis, influenza-like symptoms (fever, cough, sore throat, muscle pains), and lower respiratory disorders (pneumonia) that need to be hospitalised. On the other hand, a variety of diseases have been connected to human HPAI A virus infections. The spectrum of illnesses has included severe respiratory illnesses, influenza-like illnesses, and conjunctivitis alone.

**Pathogenesis**

Extremely harmful to birds Depending on the strain and host species, influenza virus strains can display varying pathobiologies, but they can cause substantial morbidity and death in the majority of domestic bird species. It has been demonstrated that the developing H5- and -H7 (HPAIV) have a brief incubation period in injected embryos and are extremely pathogenic to chickens. From moderate respiratory symptoms to viremia, visceral and CNS infection, severe respiratory signs, and minimal faecal transmission, the signs caused by the Eurasian strains in ducks have changed over time. With heart and brain infections, young ducks showed high mortality. But just 1% of the titer released by infected hens is expelled by infected ducks [34]. The duck pathogenic strains' phylogenetic study did not find any changes in the analysis of the sequential subtype infections in natural reservoir species revealed that birds were protected from clinical expression and had significantly less viral excretion due to homo subtypic immunity. The heterotypic immunity, however, only slightly decreased both. Despite permitting transmission, reservoir birds' heterosubtypic immunity guarantees clinical protection [36]. After a period of three to seven days, edoema and cyanosis of the head, neck, comb, and wattle, petechial haemorrhages in serosa membranes, excessive thirst, watery diarrhoea with a greenish to whitish colour, sudden death, severe depression, ruffled feathers, lack of appetite, and a severe drop in egg production can occur in chickens and turkeys. Turkeys and chickens can have a 100% mortality rate.

**Diagnosis**

Viral nucleic acid identification by RT-PCR, antigen detection, virus culture, and measurement of increasing antibody titers can all be used to identify influenza virus in clinical specimens [7]. For routine diagnostics, subtyping is not necessary if there are no epidemiological links to areas where the H5N1 influenza virus is prevalent. However, patients with severe pneumonia of unexplained aetiology should be investigated virologically for influenza virus in countries where avian influenza H5N1 virus is known to be active. If the investigation yields positive results, the case should be further investigated using H5-subtype-specific assays in order to initiate appropriate treatment, infection control measures, and epidemiological investigations at the appropriate time [21].

Consequently, quick diagnostic tests that differentiate between influenza virus subtypes are required. Given the identification of the virus and the discovery of viral RNA in respiratory samples obtained from patients infected with H5N1 up to 16 days after the onset of sickness, it is evident that the virus may be present in the body and shed for an extended duration. The H5N1 virus has been detected using nasopharyngeal aspirates (NPA) as well as nasopharyngeal, throat, and nose swabs; however, due to the paucity of parallel research comparing various diagnostic specimens, it is still uncertain which is the preferred diagnostic specimen [37]. Currently recognised by WHO, the National Influenza Centre at National Public Health Laboratory (NPHL) and a

**Prevention and Control**

The first H5N1 vaccine (HPAIV) was approved for human use by the US Food and Agriculture Administration (FDA) in order to protect high-risk populations [38]. The Food and Agriculture Organisation of the United Nations produced a list of vaccine manufacturers for poultry influenza. Vaccinations may minimise the danger of infection and limit virus output, and they may be used for poultry outside of outbreak zones because animals pose a lower hygiene risk than humans [39].The FAO has recommended three categories of vaccination strategies:

A. Responding to an epidemic by destroying diseased domestic chicken and vaccinating only domestic poultry at high risk or utilising perifocal vaccination (ring vaccination).

B. Immunisation in reaction to a "trigger," following the disease's identification by surveillance studies, in regions where implementing biosecurity is challenging (e.g., high density of chicken farms).

C. Reaction to a "trigger" in regions where implementing biosecurity is challenging The two main options for managing the illness following influenza outbreaks in poultry and the potential pandemic threat posed by (HPAIV) of the H5N1 subtype are better biosecurity and the use of inactivated vaccinations.

Vaccinations against avian influenza are intended to safeguard flocks and prevent outbreaks. They can also be used as a weapon in perifocal immunisations to fight limited outbreaks of the illness. While eradication initiatives were employed in the US to manage the (HPAIV), other methods

**Public Health Impact**

Influenza A viruses cause serious illnesses in both humans and animals. Despite being a highly contagious and mostly self-limiting respiratory infection, influenza still has a high global morbidity and fatality rate in humans. Seasonal influenza-related complications cause an average of over 200,000 hospital admissions and 36,000 fatalities per year in the United States alone [44]. Avian influenza virus (AIV) is defined as "an infection of poultry by any influenza A virus, including by subtypes H5 and H7 [45]" by the World Organisation for Animal Health (OIE). Because H7 and H5 subtypes can transform into (HPAI) viruses, as seen in certain poultry outbreaks, OIE demands notification of all outbreaks of Low-Pathogenic Avian Influenza (LPAI) viruses.
LPAI that are not H5 or H7 are not considered notifiable. Certain HPAI viruses, such H5N1, have been shown to not infect certain species, like ducks, with disease. HPAI has been associated with AIV subtypes H5 and H7, which include the viruses H5N1, H7N7, and H7N3. Human infections have ranged in severity from mild (H7N3, H7N7) to deadly (H5N1) [46].Owing to the persistent spread of different strains (H5N1, H5N2, H5N8, and H7N8), avian influenza outbreaks are still a major global public health concern today. In 1955, it was established that the type A influenza viruses that cause chicken plague were real. A virus linked to the initial isolates of the fowl plague (surface antigens H7N1 and H7N7) in chickens, turkeys, and other poultry caused high mortality.

**Risk Factors for Avian Influenza Outbreak**

Danger of introduction by migrating birds: The long-distance transmission of AI viruses is greatly affected by water bird migration. A complex web of interconnecting flyways may allow for the possibility of widespread virus dispersion, but thorough fieldwork has not been able to determine whether migratory wild birds are spreading the H5N1 HPAI virus over long distances. There is currently evidence to suggest that infected birds may travel short distances while carrying the H5N1 virus, however long-distance migrations involving this strain of the virus have not been verified [64]. Wild birds infected with the AI virus usually carry the infection for up to one month. However, studies on H5N1 and several duck species indicate that virus shedding only lasts three to four days. During the breeding season, during moult, and at overwintering sites, wild birds from different areas gather in wetlands or other settings where virus transmission may occur. Because of this, birds from different flyways and areas may exchange viruses and other illnesses over the course of a year, which could hasten the spread of infectious agents across continents. During the current pandemic, the H5N1 HPAI virus has killed off numerous wild bird species, but no reservoir species has been found, therefore it is unclear how wild birds contribute to the disease's transmission [17].
Danger of importing poultry: At the moment, a number of countries forbid the importation of chicken and poultry products from countries where detectable artificial intelligence has been found.

It would be smart to treat all poultry products extremely cautiously, especially those that may be diseased, given the potential for disease transmission across borders. Live birds pose the greatest risk, but ill birds' dressed carcasses, contaminated fomites, poultry waste, and eggs from hens that have been affected can all spread the infection. Since fighting cocks and other recreational birds wander around and across borders, they represent a risk that should be closely controlled through legislation and inspection as opposed to outright bans, which are more likely to encourage these birds to move covertly. Similarly, prohibiting the lawful movement of live birds will not lessen the risk posed by this.Risk of transmission from infected poultry: To stop the spread of the avian influenza pandemic, surveillance programmes for both wild birds and poultry should be stepped up in nations that are currently at risk. Through better management techniques and enhanced biosecurity measures in poultry production enterprises, particularly small and "open-air" facilities where poultry and waterfowl mix with wild birds or local resident bridge species, resources should be directed towards reducing close encounters between humans, poultry, and wildlife. In general, influenza viruses thrive in water, especially in colder areas, and are easily transmitted via fomites. Moreover, several duck species have the capacity to harbour influenza viruses without displaying any symptoms of illness. Everyone who works with chickens needs to improve their hygiene considerably.

procedures after HPAI is discovered in a country's marketing landscape. This serves to both keep the virus out of an area that it has already infiltrated (biocontainment) and keep it from entering an operation (bioexclusion) [43]. The main ways that the virus spreads from one place to another are through the sale of infected birds to markets, the departure of wild waterfowl that have mingled with infected backyard poultry units, the wearing of contaminated clothing or footwear by those handling or selling poultry, and the transfer of contaminated cages and egg crates to markets or poultry farms. Therefore, communities and poultry keepers need to take preventative steps to avoid introducing the virus and lower the danger of disease spread.Environment for virus survival: Low relative humidity and low temperature in aerosols extend the life of influenza viruses, but low temperature and high moisture content in faeces shorten their survival span. The majority of research on the environmental persistence of viruses has been conducted in colder northern regions, with the following results (Martin, 2006). The AI virus can endure up to five weeks in the environment of a chicken home and at least 35 days in faeces kept at 4°C. The virus can survive in lake water for up to 4 days at 22°C and more than 30 days at 0°C. The influenza virus is susceptible to several disinfectants and stable throughout a pH range of 5.5-8.

## Conclusion

Avian influenza virus strains have been dispersing and changing within wild bird populations. Because avian influenza viruses are species-specific, they seldom transcend species boundaries. However, human infections have occasionally been caused by subtypes H5, H7, and H9, usually as a result of intimate contact with sick birds. AI outbreaks could have a significant negative economic and social impact on the chicken industry, trade, and public health. The significant economic impact of HPAI outbreaks is attributed to a number of factors, including the cost of replacing and culling birds, customer unhappiness, losses in domestic and international trade, the cost of biosecurity, and the cost of veterinary care and infrastructural improvements. Embargoes on international trade hurt every part of the poultry sector in a nation. The implementation of management practices that integrate personal hygiene, cleaning and disinfection procedures, immunisation, cooking and processing standards, and biosecurity ideas can help control the spread of AI viruses. The H5N1 HPAI viruses pose the greatest threat to public health due to human infections and deaths that occur from close contact with infected poultry, whether they are living or dead. H5N1 HPAI viruses have sporadically infected humans, primarily (60%) for infections in humans.

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