Animal Influenza: An Eco-Health Outlook

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ABSTRACT

Animal influenza is a contagious respiratory disease caused by influenza viruses of the family Orthomyxoviridae that are further classified into types A, B, C and D. Influenza viruses can infect many species of mammals including humans and birds. They pose a significant threat to public health considering their zoonotic potential. The influenza viruses, mainly type A, tend to rapidly evolve through antigenic drift and shift resulting in viral miscellany that can potentially give rise to novel strains with zoonotic and pandemic potential. The trait of genetic reassortment and versatility of these viruses make it challenging to understand their transmission patterns, genetic modifications, vaccine development, and control measures. Avian influenza viruses and Swine influenza viruses have epidemiological significance because of their history of endemic and pandemic outbreaks. The effects of animal influenza outbreaks on economics, and agriculture, together with the potential for zoonotic transmission, highlight the importance of comprehensive monitoring, vaccination strategies and combined efforts among veterinary, public health, and research communities to address the challenges effectively. This chapter provides a detailed analysis of the key aspects of animal influenza following recent research, covering its etiology, transmission dynamics, viral ecology, host-pathogen interactions, epidemiology, zoonotic potential, and acquittal strategies for the well-being of animal and human populations.

Keywords: Animal Influenza, Zoonotic Potential, Influenza A viruses, Epidemiology

CITATION

Kiran B, Bukhsh A, Naqvi FZ, Somal S, Naeem RF, Pasha RH and Zafar MA, 2023. Animal influenza: an eco-health outlook. In: Aguilar-Marcelino L, Zafar MA, Abbas RZ and Khan A (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 3: 13-28. https://doi.org/10.47278/book.zoon/2023.82

CHAPTER HISTORY Received: 10-July-2023 Revised: 20-Aug-2023 Accepted: 09-Sep-2023

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1. INTRODUCTION

Animal influenza is an infectious, transmissible respiratory disorder of global importance in mammals and birds caused by influenza viruses. Influenza viruses belong to the Orthomyxoviridae family. Due to their zoonotic potential, they are liable to cause a severe and significant threat to global public health in both animals and humans. Influenza viruses cause infection in humans and many species of animals such as birds, horses, dogs, pigs, etc. Interspecies transmission of their viral strains can occur which may lead to the spread of endemic or pandemic influenza virus infection among populations (Usman and Maimuna 2009).

The evolving nature of influenza viruses leads to the constant emergence of new variants and strains. This constant genetic variation of influenza viruses is considered to be their unique trait among respiratory tract viruses (Webster 2002). This behavior of influenza viruses results in the rise of epidemics and sometimes pandemics of varied intensities. There is a recommended system of nomenclature by World Health Organization according to which viral strains of the influenza viruses are named based on name of the species they are isolated from, their year of isolation, and their genus (Mostafa et al. 2018; Memorandum 1980).

2. OVERVIEW OF ANIMAL INFLUENZA VIRUSES

2.1. ETIOLOGY

Influenza viruses belong to the family Orthomyxoviridae, Order Articulavirales, and Phylum Negarnaviricota Influenza viruses are classified into four genera Alphainfluenzavirus, Betainfluenzavirus, Gammainfluenzavirus, and Deltainfluenzavirus based on the antigenic differences of their surface proteins, i.e., nucleoproteins (NP) and matrix 1 (M1) proteins. Each of these genera has only one species, which are named influenza A virus (IAV), influenza B virus (IBV), influenza C virus (ICV), and influenza D virus (IDV), respectively (Kuhn et al. 2020; Mostafa et al. 2018).

2.2. MORPHOLOGY AND STRUCTURE

Influenza viruses are observed to be pleomorphic. They exhibit elliptical, spherical or filamentous shapes with a diameter of 80–120 nm and a length up to 20 µm. The influenza virus is enveloped with a lipid-bilayer membrane. The outer layer of virion possesses matrix protein M2 ion channels and embedded spike-like projections of viral proteins. Influenza viruses A and B are almost similar in structures. IAV and IBV have spikes of hemagglutinin and neuraminidase (Vijayakrishnan et al. 2013). While ICV and IDV have distinguished spike-like reticular structures known as hemagglutinin esterase fusion (HEF) glycoprotein, arranged in hexagonal patterns. They have chimeric M2 (CM2) instead of M2 in their outer layer. CM2 is closely related to M2 of IAV (Su et al. 2017).

The inner layer of the virion is an envelope of matrix protein M1 that provides firmness to the outer layer. Underneath the inner layer, nuclear export protein (NEP) is attached to M1 layer. Center of the virion comprised eight viral ribonucleoprotein (vRNP) structures organized as one central long vRNP surrounded by seven vRNPs. vRNPs are single-stranded RNAs connected with polymerase complex and lined with nucleoprotein. Unlike IAV and IBV, the core of ICV and IDV have seven vRNPs instead of eight (Fig. 1) (To and Torres 2019).

2.3. GENOMIC CONFIGURATION OF INFLUENZA VIRUSES

Influenza viruses have basically their genomes structured as segmented, single-stranded RNA molecules enveloped in nucleoprotein. They are pleomorphic, negative - sense viral RNA viruses (Barnard 2009).

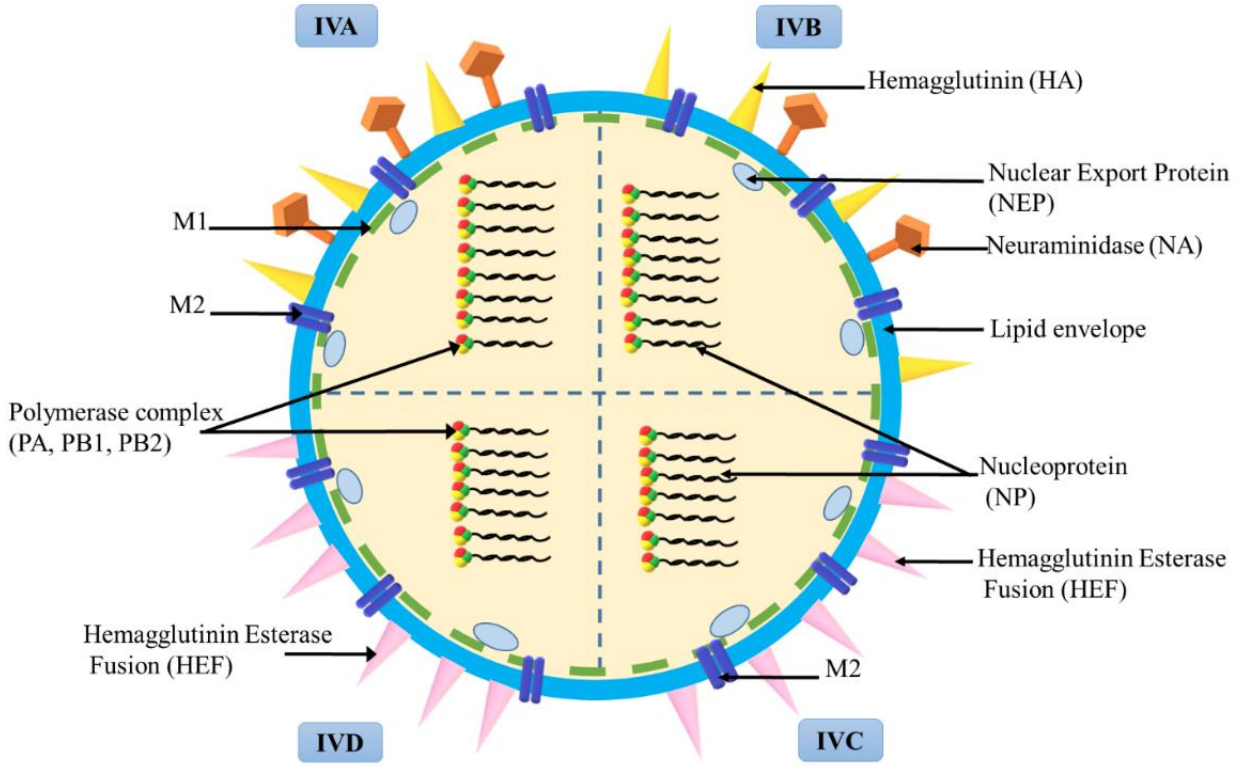

Fig. 1: Structure of Influenza viruses A, B, C and D.

The eight segments of the influenza A and B viruses can encode more than 10 proteins, named Matrix proteins (M1 and M2), Nucleoprotein (NP), Hemagglutinin (HA) glycoprotein, Neuraminidase (NA) glycoprotein, Polymerase acidic protein (PA) subunit, Polymerase basic protein1 and 2 (PB1 & PB2) subunits, and Nonstructural proteins (NS1 and NS2). These segments are named on the basis of the main proteins they encode (Parvin et al. 2022). Influenza C and D viruses contain seven segments of RNA. Three longest segments form the trimeric polymerase complex, encode polymerase basic proteins (PB1), polymerase basic 2 protein (PB2) and polymerase acidic (PA/P3) proteins. Other four segments encode hemagglutinin esterase fusion (HEF) glycoprotein, nucleoprotein (NP), matrix proteins (M1 and chimeric M2 protein (CM2)), and non-structural proteins (NS1 and NS2), respectively (Wolff and Veit 2021). Genomic sequence of the influenza D virus varies from that of the influenza C virus by 50%. There is no genetic interaction that occurs between influenza viruses C and D to form recombinants. There is also no cross-reaction recorded among their antibodies (Hause et al. 2014).

2.4. LIFE CYCLE AND PATHOGENESIS

Influenza viruses take the path of receptor-mediated endocytosis to enter the host cells. Sialic acid (SAα2,6-Gal/SAα2,3-Gal) adhered to the glycolipid and glycoproteins of the outer cell surface of most of the host cells is the binding receptor for influenza viruses. They are specified to target the epithelial cells of the upper or lower respiratory tract. However, the receptor on the targeted host cell used by the influenza C virus is 9-O-acetyl-Nacetylneuraminic acid which is an acetylated derivative (Wolff and Veit 2021). Hemagglutinin plays a significant role in receptor binding and membrane fusion during viral entry into host cells. A low pH environment is important for the initiation of fusion and M2 ion channel activation (Bedi and Ono 2019). The acidic nature of the endosome induces changes in the conformation of

hemagglutinin molecules to initiate the process of fusion of membranes i.e., membranes of virus and membranes of endosomes. This fusion of membranes then results in the release of viral ribonucleoproteins (vRNPs) in the cytoplasm of the host cell. After entering the nucleus from the cytoplasm through nuclear pores, these vRNPs act as transcription templates (Dadonaite et al. 2019). Viral polymerase complex (polymerase basic 1, polymerase basic 2 and polymerase acidic subunits) transcribes the viral RNAs to messenger RNAs for the production of viral proteins (Neumann and Kawaoka 2015). Replication of viral RNA and transcription of mRNA occurs in the nucleus, while the translation of viral protein takes place in cytoplasm. Newly generated vRNPs are then actively released in the cytoplasm with the help of non-structural proteins 2 (NS2) or nuclear export protein (NEP). Hemagglutinin, neuraminidase, M1 protein, M2 protein and vRNPs are needed to be transferred to the plasma membrane for the assemblage of new virus and budding (Su et al. 2017). Lipid raft domains located in plasma membranes of the host cells are used as replication sites by viruses. Neuraminidase plays an enzymatic role in the release of new viruses from the infected host cells by cleaving the binding receptors (Rossman and Lamb 2011). Non- structural proteins 1(NS1) play a vital role in the immune system circumvention of the host (Dou et al. 2018). In the case of influenza viruses C and D, instead of HA and NA, hemagglutinin esterase fusion protein (HEF) plays role in the viral entry of viral RNA in the host cell by membrane fusion, receptor binding, and cleavage of binding receptors during the exit stage of the newly produced virus (Hause et al. 2014).

After their release from the host cell, they start to invade other surrounding cells. Temperature sensitivity of influenza C viruses reduces the production of their new virions at higher temperatures. That is why they infect the upper respiratory tract more than the lungs where the temperature is high. Influenza D viruses are found to be more temperature stable than influenza A, B, and C type viruses (Wolff and Veit 2021).

Apoptosis of infected host cells by influenza virus occurs after the exit of newly produced viruses from host cells through direct triggering of NS2 and PB1-F2 viral protein. The incubation period of influenza virus is 1 to 4 days (Peaper and Landry 2014). Influenza virus infection causes oxidative stress which leads to neutrophil infiltration and high production of reactive oxygen species resulting in tissue damage. There is a rapid production of cytokines by epithelial cells and immune cells of respiratory mucosa as an immune response in severe influenza virus infection. Their overexpression results in high level lung tissue edema, pneumonia, hemorrhage of alveoli or may result in multiple organ failure (Luo et al. 2023). Influenza A virus infection escalates levels of metabolites in plasma and urine (Francis et al. 2019) (Fig. 2).

3. AN ECO-HEALTH OVERVIEW OF ANIMAL INFLUENZA VIRUSES

3.1. INFLUENZA A VIRUS

Influenza A viruses are considered to be the most common and highly pathogenic among all the other influenza viruses. They display high levels of morbidity and mortality in birds and mammals. IAVs are also zoonotic in nature, i.e., they can transmit from animal hosts to humans. Aquatic birds are naturally the host reservoir of the influenza A viruses. Mammals in which influenza A viruses have been reported include pigs, horses, dogs, bats and humans (Wille and Holmes 2020) (Fig. 4).

3.1.1. SUBTYPES

Influenza A viruses are further categorized into different subtypes on the basis of their antibody response and their surface proteins, hemagglutinin and neuraminidase (Usman and Maimuna 2009). These proteins have their role in host cell entry and exit of virion during the replication process. Eighteen known hemagglutinins (H1- H18) and eleven neuraminidases (N1- N11) are there. Viruses containing H1 to H16 hemagglutinin and N1 to N9 hemagglutinin appeared to cause infection in birds (Capua and Munoz 2013).

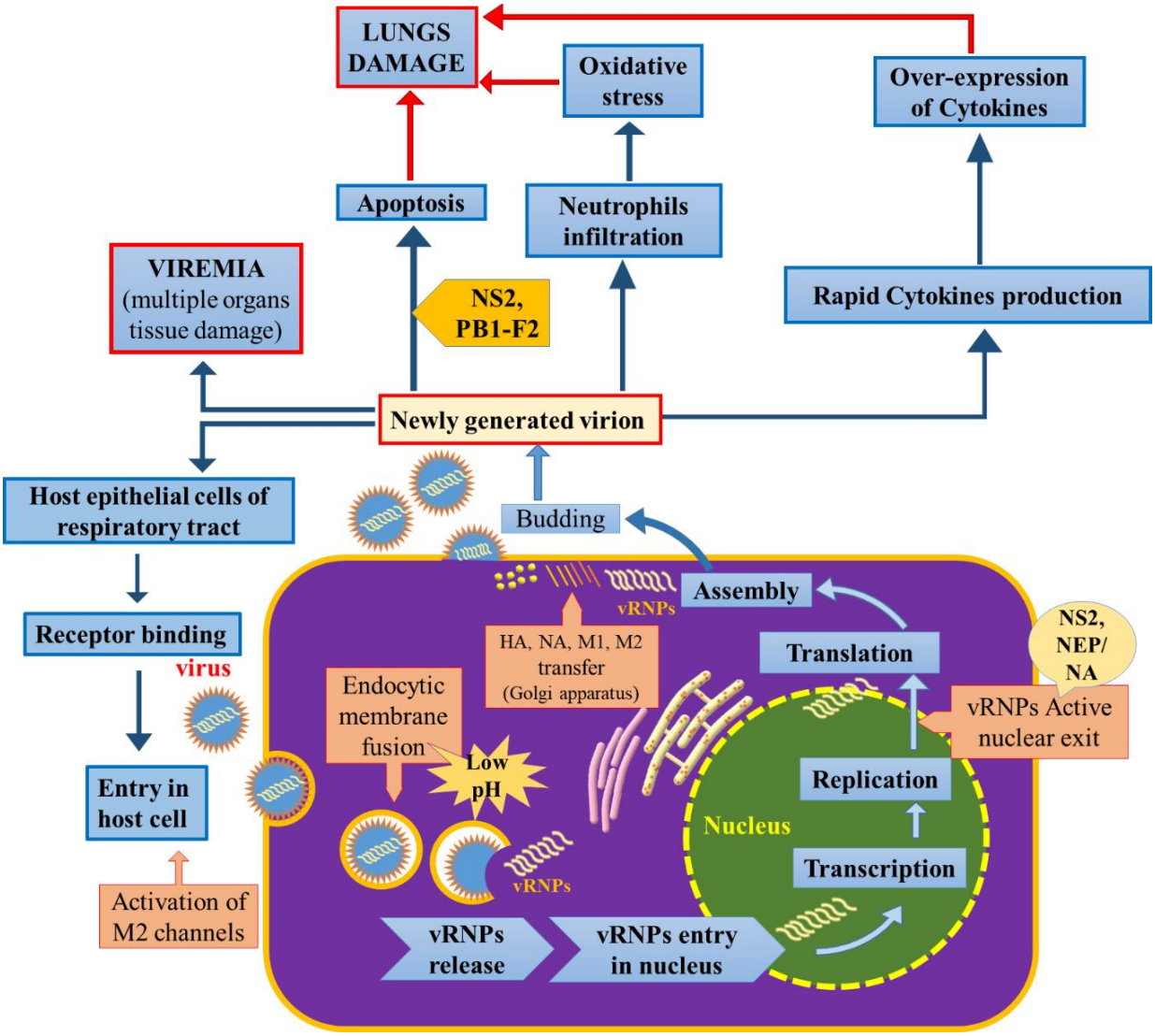

Fig. 2: Schematic representation of life cycle and pathogenesis of influenza virus.

3.1.2. ANTIGENIC SHIFT AND DRIFT

Influenza A viruses show phenomenon of "antigenic drift" that refers to a gradual change in hemagglutinin and neuraminidase of virus. This process results due to influenza A virus's ability of enduring minor to major variations in its genome. Major changes in hemagglutinin and neuraminidase proteins lead to the nullification of existing immune responses of host against that virus. The changes will be major and rapid if virus undergoes genetic reassortment (Collisson et al. 2007). It can even result in a whole new hemagglutinin and/or neuraminidase. These sudden and major changes in virus result in emergence of novel influenza viruses. This process is referred to as "antigenic shift" (Heinen 2002; Spickler et al. 2008) (Fig. 3).

3.1.3. AVIAN INFLUENZA A VIRUSES

Avian influenza A viruses (AIVs) are very diverse and heterogenic in nature, with highly variable sixteen hemagglutinin and nine neuraminidases. Among the subtypes of avian influenza, the H9N2 subtype is

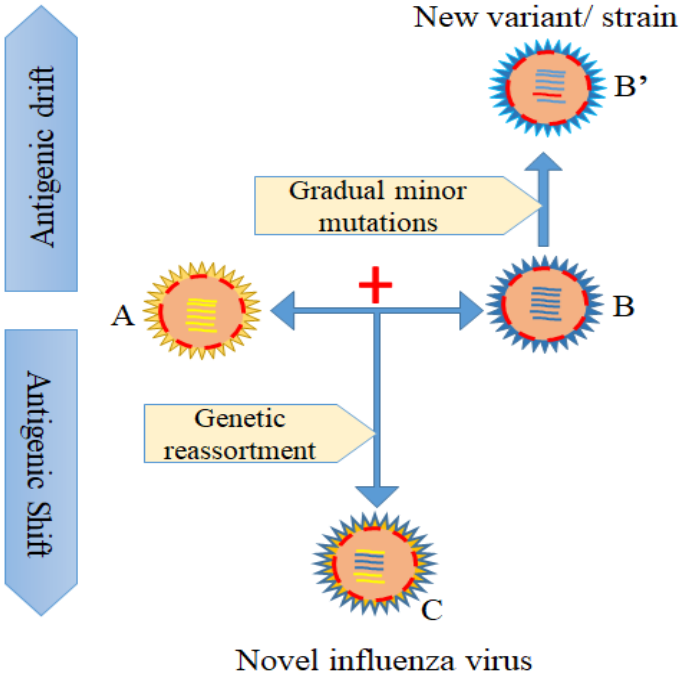

Fig. 3: Antigenic shift and antigenic drift.

considered to be the most prevalent and appears to be causing infection globally (Xu et al. 2018). AIVs target α2,3-SA receptors for binding. Although α2,6-SA receptors are abundant in respiratory and intestinal tracts of birds but very few AIV H16N3 (gull), in poultry H9N2 and H7N2, and H6N6 from duck showed binding potential for these receptors (Liu et al. 2023). Over the past twenty years, the sporadic zoonotic spread of the avian influenza virus has instigated concern regarding the incidence of the virus in poultry and poultry products. This concern was raised due to the occurrence of widely fatal pandemics and infectious outbreaks of avian influenza viruses reported in humans. These outbreaks are the cause of intense socio-economic losses (Naguib et al. 2019).

3.1.4. SUBTYPES

Avian influenza A viruses are categorized into two groups on the basis of their virulence in poultry i.e., Low pathogenic avian influenza viruses (LPAI) and high pathogenic avian influenza viruses (HPAI).

HPAI and LPAI viruses have a structural difference in their hemagglutinin protein and its cleavability. LPAI virus hemagglutinin cleavage is mediated by trypsin-like enzymes. These enzymes are present in respiratory secretions and epithelial cells. Therefore, usually, LPAI viruses remain at the sites present in the gastrointestinal and respiratory tracts. While HPAI viruses undergo cleavage of their hemagglutinin with the help of furin enzymes which can be found in the whole body. Therefore, HPAI virus infection involves multiple organs and systems of the body resulting in severe infections in the host (Swayne 2007). They can show high mortality and morbidity rates. Birds already infected with other pathogens, sick or stressed due to external factors are more likely to get infected by LPAI viruses (Spickler et al. 2008). Most of the avian influenza viruses are low pathogenic. They cause mild infections in birds. Low pathogenic viruses having hemagglutinin H5 or H7 may undergo mutational changes and turn themselves into high pathogenic viruses (Naguib et al. 2019). Low pathogenic influenza viruses can stay in their hosts for long periods, reassorting and producing novel variants. Some HPAI viruses are not highly pathogenic or non-pathogenic in chickens. These viruses can eventually undergo evolution and become more virulent (Patapiou et al. 2022).

3.1.5. CLINICAL SIGNS AND SYMPTOMS

Clinical signs and their intensity during HPAI infection normally vary with the virus. It is said that avian influenza viruses have a high mortality rate and cause the instant death of birds. The mortality rate can reach up to 100% (Alexander 2000). Therefore, leaving very narrow chances to observe birds for the onset of clinical signs. Reportedly, the death of the infected birds was observed within 48 to 7 hours after the onset of early clinical signs. Calculating the time between onset of infection and initial mortality is difficult. This can be calculated in experimentally infected birds by measuring the average time to death. This average is known as mean death time (MDT) which depends on route, dose and subtype of virus (Swayne and Pantin 2006). Avian influenza virus has an incubation period of 48 hours up to 4 days (Khan et al. 2021). Early signs observed were tremors, nervous signs, lethargy and anorexia. Some birds reportedly showed mild respiratory signs such as petechial hemorrhages on the hock and cyanosis of wattles and comb. Respiratory signs included inflammation of the trachea, hemorrhages in the trachea, coughing, reduced vocalization, and rales were heard during clinical examination of sick birds. Nervous signs that were observed included incoordination, torticollis, paralysis and depression. Other clinical signs include severe diarrhea or greenish fecal matter, conjunctivitis, excessive lacrimation, decreased quantity and quality of eggs, huddling, ruffled feathers, haematochezia, and facial edema (Spickler et al. 2008).

3.1.6. ROUTE OF TRANSMISSION

The natural route of transmission in humans and birds for avian influenza viruses is the respiratory route. Avian influenza virus tends to zoonotically transmit through direct interaction with infected birds, respiratory secretions, or corpses of infected birds. Respiratory transmission of the virus by respiratory droplets through the conjunctiva and nostrils is an important route in humans (Sun et al. 2020). The virus sheds out of the host bird through body secretions and feces. The virus is then transmitted by air through water vapors when they come in contact with dried fecal material or feathers of infected birds. Fine droplets can pass the virus to the lower respiratory tract causing severe infections. Transmission of the virus from poultry products to the host e.g., meat and eggs is also a viable and concerning route (Rimmelzwaan et al. 2006).

3.1.7. EPIDEMIOLOGY

Avian influenza virus, because of its diversity and zoonotic significance, results in major epidemic outbreaks. These outbreaks are life threatening and eventually result in huge economic losses. Over the years, many outbreaks of the avian influenza virus have been reported displaying worldwide severe respiratory signs and a very high mortality rate. H9N2 (1998), H7N3 (1995, 1998, 2001-2002) and H5N1 (2006-2008) in Pakistan, H4N8 outbreak in Alabama in 1975, H5N2 (1983 to 1984) Pennsylvania, 1999 to 2000 H7N1 outbreak in Italy, H5N1 outbreak in Thailand (2005), H7N7 in The Netherlands in 2003, H6N2 LPAI outbreak in California 1985, H7N7 outbreak in Australia (Spickler et al. 2008; Siddique et al. 2012).

3.1.8. ZOONOTIC ASPECT

A number of avian influenza viruses made a successful way through the species, causing zoonotic infections. H10N7, H10N8, H9N2, H7N9, H7N7, H7N4, H7N3, H7N2, H6N1, H5N8, H5N6, H5N1 and H3N8 subtypes are of high significance regarding zoonosis, reportedly. They cause mild to fatal infection and in some cases, there is no display of symptoms during infection (Pusch and Suarez 2018). Sneezing and fever are mild infection symptoms in humans that are normally self-limiting. Severe illness can occur if the individual has a

compromised immune system or the attacking virion is highly pathogenic such as H7N9. Animal Influenza viruses spread pandemically when their novel virion attains the capability to transmit to humans efficiently (Sun et al. 2020). Avian influenza viruses possess the potential to become a pandemic threat if they go through some mutations so that they can replicate in mammalian cells efficiently. The three worldwide influenza pandemics; H1N1 AIV 'Spanish flu' (1918 –1919), 'Asian flu' (1957–1958) and 'Hong-Kong flu' (1968 –1969) caused by the H3N2 virus caused high morbidity and mortality, depression and socio-economic losses globally. Widespread low pathogenic H9N2 in Asia and highly pathogenic H5N1 in poultry can result in a zoonotic situation (Zowalaty et al. 2013). Co-infections with avian influenza viruses have been reported often, such as H5N1 with H9N2 and Newcastle disease and H5N1 with Newcastle disease (Channa et al. 2021).
The relation of live bird markets with the spread of avian influenza viruses is quite evident. These markets provide a stable environment for the growth, stability and transmission of different viruses. The presence of multiple species at such places provides enough opportunities for genetic exchange and mutations among viruses for the emergence of novel viruses. In keeping all the factors in view, live bird markets play a vital role in zoonotic transmission (Ali et al. 2021). It is not necessary that a virus show low pathogenicity for both birds and humans. Some avian influenza viruses can be fatal in humans but show low pathogenicity in chickens e.g., H7N9. A rare human-to-human transmission of avian influenza virus occurs. In cases of H5N1, H7N9 and H7N7 a very limited transmission of poultry-based viruses among humans has been reported (Abdelwhab and Mettenleiter 2023).

3.1.9. TREATMENT AND PREVENTION

Prevention of the spread of highly pathogenic avian influenza viruses in birds and mammals is a huge assignment. Implementation of stern rules and regulations for poultry import and export across borders,

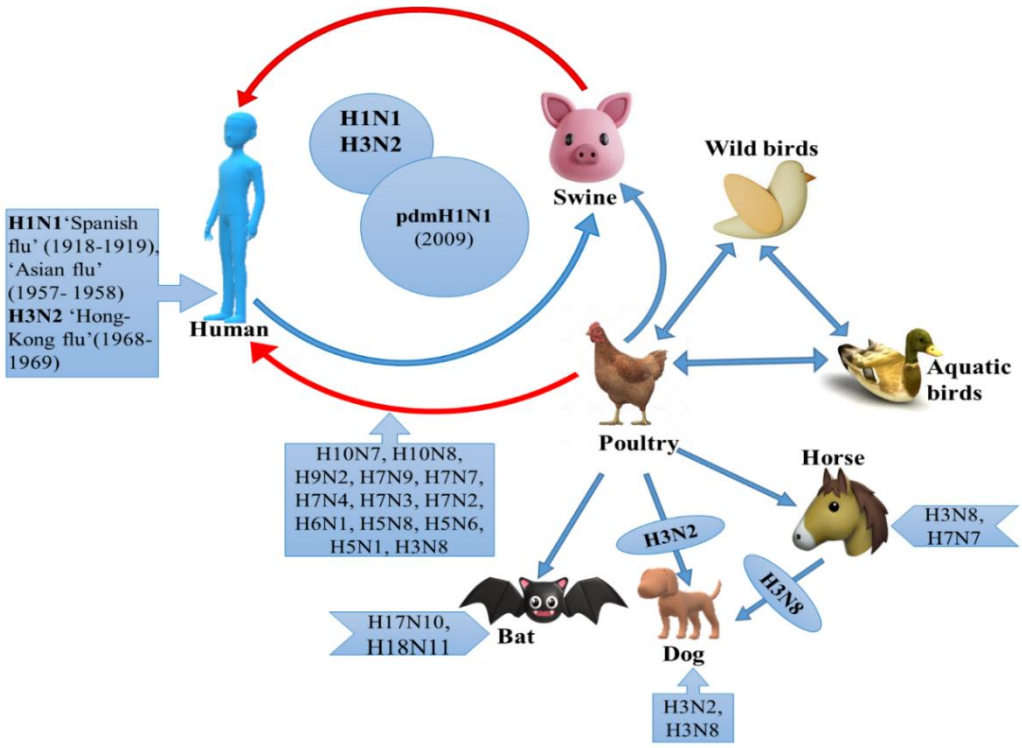

Fig. 4: Schematic flow chart for transmission pattern of influenza A viruses.

proper handling of birds, sanitization, personal hygiene, reducing direct contact with birds using safety gadgets, and vaccination are crucial precautionary steps. H5 vaccines are used in poultry to prevent virus onset, but H5 vaccines are not yet licensed in humans. Vaccine development for humans and animals is under process. Because of their evolving nature, the new pandemic strain would be antigenically modified, requiring a new type of vaccine to develop for its control. Antiviral chemoprophylaxis can be used during outbreaks for protection in high-risk individuals (Wong and Yuen 2006).

3.1.10. SWINE INFLUENZA A VIRUS

Swine influenza A viruses have vast and diverse strains. The diversity of strains is because of repeated reassortments due to the interaction of swine influenza A virus with avian influenza A virus and human influenza A virus. The genetic constitution is still restricted to subtypes H1N1, H1N2, and H3N2. Ancestral European avian-like (EA) H1N1 swine influenza A virus showed affinity for both sialic acid receptors, unlike the human H1N1 virus, due to their evolved antigenic difference (Liu et al. 2023). Pigs are hosts for the swine influenza A virus, where these viruses reassort with avian influenza viruses and human influenza A virus. This reassortment results in the emergence of novel viruses and pandemics e.g. pdmH1N1 contains gene segments from the avian influenza virus, human influenza A virus and swine influenza A virus (Abdelwhab and Mettenleiter 2023).
Swine have both types of sialic acid receptors distributed in the respiratory tract that are possessed by avian and humans. α2,6-SA receptors in the trachea and bronchus are more than α2,3-SA, while both are equally distributed in the bronchioles and alveolar region. Both receptors were also found to be sited in other organs, including the digestive tract, kidneys, liver, heart, brain and skeletal muscles. Therefore, they can infect multiple systems in the body (Nelli et al. 2010).

3.1.11. ROUTE OF TRANSMISSION

Swine influenza A viruses can be transmitted zoonotically through direct contact between pigs and humans. However, the globally reported infection rate in humans of swine influenza A virus is lower than that of avian influenza viruses. Transmission of human influenza A virus to pigs leads to the formation of a reservoir for influenza A viruses of zoonotic significance in pigs (Abdelwhab and Mettenleiter 2023).

3.1.12. CLINICAL SIGNS

Humans and pigs showed almost similar clinical signs for swine influenza A virus infection. Therefore, pigs can effectively be used as study models for influenza viruses. Fever, lethargy, anorexia, respiratory distress, nasal discharge, coughing, conjunctivitis, and sneezing are common characteristic symptoms of swine influenza A virus (Heinen 2002). The incubation period of the virus is 1 to 3 days. The onset of infection is usually sudden. Swine influenza is characterized by almost 100% morbidity but has low mortality in pigs (Vincent et al. 2008).
Swine have receptors for both humans and birds; therefore, they are considered to undergo reassortment between human influenza viruses and avian influenza viruses. That is the reason swine are generally termed as potential mixing vessels for reassortment (Abdelwhab and Mettenleiter 2023).

3.1.13. EPIZOOLOGICAL ASPECT

Swine influenza viruses prevalent in pigs can transmit zoonotically and cause severe pandemics. Swine influenza A virus presence in pigs was first identified in 1918 during the Spanish flu pandemic. In 1930 first

swine influenza virus was isolated by Shope in 1930 was from the H1N1 lineage now known as classical swine H1N1. In 2009, the first 21st century pandemic occurred involving the global spread of swine-origin H1N1 influenza A virus infection. H1N1 swine influenza A virus is a blend of swine, human and avian influenza A viruses due to multiple reassortment between them (Zowalaty et al. 2013).

Classical swine H1N1 can be widespread among the major pig populations of the world, getting 25% of the population infected. In Europe, in 1979 antigenically distinct from classical swine H1N1 viruses, avian-like swine H1N1 viruses were recognized. H3N3 human influenza virion appeared in pigs during 'Hong Kong flu' pandemic around 1970. This human influenza virus after reassortment with avian-like H1N1 swine virus generated a new human-like swine H3N2 influenza virus with structural and genomic properties of human and avian. This virus can cause serious illnesses and can spread rapidly. The H1N1 virus pandemic in 2009, caused sporadic infections (Heinen 2002; Garten et al. 2009).

Due to sporadic infections, vast diversity and frequent reassortments among viral strains in swine, and low immunization of populations towards new strains, the chances of an outbreak of a pandemic are always higher. Several organizations are working as a unit to identify new forming strains of swine influenza viruses pre-pandemic (Rambo-Martin et al. 2020).

3.1.14. EQUINE INFLUENZA A VIRUS

Equine influenza A viruses cause respiratory tract infections in horses and other equines. H3N8 and H7N7 are two subtypes of equine influenza A virus that kept on causing infections in equines. But after 1970s, no known cases of H7N7 have been reported. H3N8 viruses are still prevalent in horses causing sporadic infection and keep on evolving to form new lineages. H1N8, H5N1, H7N1, and H9N2 are the other influenza A viruses that have been found in horses. Zoonotic transmission of equine influenza A viruses has never been confirmed. However, the presence of viruses in humans with no notable infection has been reported several times worldwide i.e., in 1959, 1965, 1960s, 1963, 1965, 2005, 2008 to 2013, 2014 and 2015 (Abdelwhab and Mettenleiter 2023). It has been reported that there is a limited transmission of the H3N8 equine influenza A virus in other mammals like dogs, cats, pigs and camels. Fever, mild flu-like symptoms and seroconversion have been observed in equine Influenza virus-infected individuals (Borkenhagen et al. 2019).

3.1.15. CANINE INFLUENZA A VIRUS

H3N8 and H3N2 canine influenza A virus subtypes, isolated in 2000s, were observed to infect only dogs. But dogs are not natural hosts for influenza A virus. The outbreak of the H3N8 canine influenza virus in dogs which was related closely to the equine influenza H3N8 virus, was reported for the first time in 2002 in UK (Abdelwhab and Mettenleiter 2023). H3N8 canine influenza virus is a genetic divergent of the equine influenza virus and is avirulent towards horses. Several outbreaks of canine influenza viruses have been reported over the years. In 2005 another subtype H3N2 having avian-origin gene segments was isolated from dogs. H3N2 canine influenza virus can be transmitted to cats. Zoonotic transmission of H3N8 or H3N2 canine influenza virus is considered to be very low (Borkenhagen et al. 2019).

3.1.16. BAT INFLUENZA A VIRUS

H17N10 and H18N11 viruses were isolated in 2009 to 2011 from bats. These viruses do not infect other species. They are unique in their hemagglutinin H17 and H18 structure and binding properties. Their

internal genes are unique from other influenza A viruses. To date, no zoonotic transmission of bat influenza viruses has been confirmed (Abdelwhab and Mettenleiter 2023).

3.2. INFLUENZA B VIRUS

Influenza B viruses (IBV) primarily infect humans. There are two IBV strains Victoria and Yamagata. This strain can genetically reassort and have limited antigenic cross-reactivity. Other animals prone to IBV are seals *(Phoca vitulina).* They show low rates of evolution. Clinical symptoms displayed by IBV are flu-like symptoms. IBV are not much genetically diverse, due to which level of immunity can be attained. Therefore, the potential of IBV to cause a pandemic is very low. But they are known to cause seasonal outbreaks. IBVs can be efficiently prevented by vaccination (Wolff and Veit 2021).

3.3. INFLUENZA C VIRUS

Influenza C viruses have humans as primary hosts but they are also found in farmed pigs. ICVs infections are asymptomatic or may cause mild respiratory distress, Inflammation of the upper respiratory tract, fatigue, cough and fever. In pigs, the infection can be sustained for a month approximately (Hause et al. 2014).
ICVs are distributed worldwide. The transmission of the virus occurs through respiratory route. Human-to-human transmission of ICVs is efficient. They can cause persistent infections in human populations. Isolation of influenza C virus from an infected human in 1947 revealed that ICVs do not show cross-reactivity against IAV or IBV antibodies. ICVs are not life-threatening. Therefore, vaccines have not been developed for ICVs (Wolff and Veit 2021).

3.4. INFLUENZA D VIRUS

Influenza D virus (IDV) in 2011 was identified in swine showing influenza-like clinical signs and then subsequently in cattle. Cattle is the only reservoir of IDV. IDV is the first identified influenza virus in cattle (Hause et al. 2014). IDV and ICV having genetic similarities emphasize IDV being a descendant of ICV for 300 to 1500 years. IDV also infect other mammals naturally such as horses, sheep, goat, camel and pigs (Ferguson et al. 2016). Interspecies transmission of IDV can occur through direct contact. Distribution of IDV is worldwide. There is no indication of zoonotic transmission of IDV. IDV infects ferrets, which are the favored human alternate animal models for influenza virus studies. In vitro analysis of IDV revealed their ability to grow and replicate on human airway cell culture (Abdelwhab and Mettenleiter 2023). Also, IDV has a broad cell tropism because of its HEF glycoprotein's open receptor-binding cavity. These characteristics of IDV point towards its potential for zoonosis (Ferguson et al. 2016).

4. EVOLUTION OF ANIMAL INFLUENZA VIRUSES

Influenza viruses have segmented genomes that allow genetic exchange among different strains. This property is considered helpful in the evolutionary process (Wolff and Veit 2021). The emergence of new subtypes and strains of animal influenza remained a significant concern for global health (Lowen 2017). One of the major concerns with animal influenza is the potential for reassortment, a process in which genetic material from different influenza viruses combines to form a new subtype with the potential to cause a pandemic if it gains the ability to spread efficiently among humans. Vigilant surveillance and rapid identification of emerging subtypes and strains are crucial for early detection and response (Wille and Holmes 2020).

Monitoring high-risk areas and animal populations, especially those in close proximity to humans, is essential for detecting emerging subtypes and strains. Genetic sequencing and characterization of the viruses provide insights into their pathogenicity, antigenicity, and potential for human transmission. Continuous monitoring of viral evolution and the identification of genetic markers associated with increased virulence or adaptation to new hosts can guide the development of targeted interventions (Reperant et al. 2012).

5. ONE HEALTH APPROACH TO ANIMAL INFLUENZA

Human development has increased carbon emissions, causing a rise in global temperature. The rise in temperature, deforestation, increased humidity, pollution, and overpopulation destroyed the lifecycles and diversity of ecosystems. These factors, along with increased direct contact with animals due to urbanization enhanced threats of zoonotic transmission of diseases (Yasmeen et al. 2022). Environmental considerations play a significant role in the emergence, spread, and persistence of the virus (Naguib et al. 2019). Key aspects include:

- Wild bird ecology: Wild birds, particularly waterfowl, are natural reservoirs of avian influenza viruses and play a crucial role in the virus's ecology and transmission. Studying their migratory patterns, habitats, and interactions with domestic birds is important for understanding the dynamics of virus circulation.
- Environmental contamination: The virus can persist in the environment, such as in water bodies or contaminated surfaces. Environmental monitoring and assessing the survival and transmission potential of the virus in different settings help inform control measures and risk assessment.
- Climate change and land-use changes: Environmental changes, including climate change and land-use changes, can impact the distribution and behavior of avian influenza viruses and their hosts. Understanding these dynamics helps anticipate and mitigate the risks associated with changing environments.
- Environmental health interventions: Implementing environmental health interventions, such as proper waste management, water treatment, and hygiene practices, can reduce the risk of environmental contamination and transmission of the virus.

5.1. DIAGNOSIS

Detection of viral strain is important in the diagnosis of influenza viruses to take essential clinical steps to prevent the virus. Samples in the form of swabs or tissue collected for testing. Reverse transcription-polymerase chain reaction (RT-PCR) is considered a strong and preferred diagnostic test for influenza viruses (Khan et al. 2021). Other detection tests include rapid influenza diagnostic tests, ELISA, hemagglutination inhibition test for antibodies detection, Immunofluorescence method for antigen detection, fluorescent antibody staining assays, and viral culture method (Patapiou et al. 2022).

5.2. TREATMENT, PREVENTION AND CONTROL STRATEGIES

Virus propagation in a population depends on host species, viral subtype, season, geographical location, and vaccine efficiency (Zaman et al. 2019).

5.3. VACCINATION

Vaccination is an essential tool for preventing and controlling animal influenza. Vaccines can be developed for specific strains of influenza viruses to reduce the risk of infection and disease in both animals and

humans. Vaccination programs are commonly used in domestic poultry to minimize the spread of avian influenza viruses and protect bird populations (Patapiou et al. 2022). Vaccination strategies include the use of inactivated vaccines, live attenuated vaccines, or recombinant vaccines. Inactivated vaccines are typically administered via injection and provide protection against specific strains of the virus. Live attenuated vaccines are administered orally or by aerosol and mimic a natural infection, stimulating an immune response. Recombinant vaccines use genetic engineering techniques to produce viral antigens and stimulate an immune response. Vaccination of poultry can reduce the severity of the disease, decrease viral shedding, and limit transmission to humans (Dey et al. 2023). However, vaccination alone is not sufficient and should be combined with other control measures such as biosecurity practices and surveillance.

5.4. ANTIVIRAL MEDICATIONS

Antiviral medications can be used as a control strategy for animal influenza, particularly in situations where vaccination is not feasible or as a complement to vaccination. Antiviral drugs, such as neuraminidase inhibitors (e.g., oseltamivir, zanamivir), can help reduce the severity and duration of illness, as well as limit viral replication and transmission (Luo et al. 2023). Antiviral treatment is typically recommended for infected individuals or individuals with a high risk of exposure, such as healthcare workers caring for patients with confirmed cases of zoonotic influenza. Antiviral drugs may also be used for outbreak control in animal populations. Indiscriminate use of antiviral drugs can contribute to the development of drug-resistant strains of the virus.

5.5. BIOSECURITY MEASURES

Biosecurity measures are critical in preventing and controlling the spread of animal influenza. These measures aim to minimize the introduction and transmission of the virus within and between animal populations (Mak et al. 2012). Key biosecurity practices include:

- Restricted access: Implementing strict control of access to farms, live bird markets, and other animal facilities helps prevent the entry of infected animals or contaminated materials.
- Hygiene protocols: Promoting good hygiene practices, such as hand washing, disinfection of equipment and surfaces, and proper waste management, reduces the risk of virus transmission.
- Separation and isolation: Isolating infected or potentially infected animals from healthy animals minimizes the spread of the virus. This includes separating sick animals, implementing quarantine measures, and segregating different animal species.
- Poultry production systems: Improving the design and management of poultry production systems can reduce the risk of virus introduction and spread. Measures such as improved ventilation, separate production zones, and proper waste management can enhance biosecurity.
- Surveillance and early detection: Implementing active surveillance programs to monitor animal populations for signs of infection allows for early detection and rapid response, limiting the spread of the virus.
- Slaughter and quarantine policies are crucial control measures during zoonotic outbreaks of animal influenza. These measures aim to contain the spread of the virus and prevent further transmission to humans or other animals.

5.6. PUBLIC HEALTH EDUCATION AND AWARENESS

Public health education and awareness campaigns play a crucial role in preventing and controlling zoonotic influenza. These campaigns aim to educate the public, animal handlers, healthcare professionals, and

other stakeholders about the risks of zoonotic influenza and preventive measures (Mak et al. 2012). Key components include:

- Information dissemination: Providing accurate and up-to-date information about animal influenza, including modes of transmission, signs and symptoms, and preventive measures, helps raise awareness and promote responsible behavior.
- Hygiene practices: Promoting good hygiene practices, such as regular hand washing, proper cooking of poultry products, and respiratory etiquette, helps reduce the risk of transmission.
- Risk communication: Clear and effective communication during outbreaks helps build public trust and understanding. Providing timely information about outbreaks, control measures, and recommended actions helps individuals make informed decisions.
- Stakeholder engagement: Collaborating with various stakeholders, including farmers, veterinarians, healthcare professionals, and public health authorities, ensures a coordinated response and effective implementation of preventive measures.

6. CONCLUSION

Animal influenza is a multifaceted threat with the zoonotic potential, impacting the balance of the ecosystem. This is a contagious viral respiratory disorder, considered important globally. Continuous emergence of new strains and interspecies transmission of influenza viruses may result in outbreaks. Vaccination is a vital key for the prevention and control of animal influenza. Public health education and awareness campaigns, vigilant monitoring, continued research, early detection, and rapid response are the preventive strategies for fostering an Eco- Health approach, emphasizing the interconnectedness of animal, human, and environmental health and mitigating the risks of potential zoonotic influenza endemic or pandemic among populations.

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