An Overview Of Avian Influenza In Waterbirds

Abstract

Avian influenza is an infectious disease caused by Avian (bird) Influenza (flu) Type-A viruses. These viruses are naturally found in wild bird populations, specifically in birds with affinities to aquatic habitat. The viruses can also infect domestic poultry and other bird and animals species. Two strains of AI viruses have been reported: the low-pathogenecity avian influenza (LPAI) and the highly pathogenic avian influenza (HPAI) with the latter having mortality rates close to 100%. Sporadic cases of human infections transmitted through close contact with sick/dead poultry have also been reported. Nearly, seven sub-types of AI viruses are known to infect humans. Since 2003, 15 countries have reported Avian Influenza outbreaks in humans with an overall mortality rate of nearly 58%. Comprehensive control programs have been developed to monitor avian influenza disease prevalence, spread and eradication. Sub-type specific vaccines have also been developed to protect domestic poultry from infections. With 102 reports of H5N1 outbreaks since 2006, India is one of the countries with high prevalence of avian influenza. An action plan by the Department of Animal Husbandry, Dairying and Fisheries, Government of India, outlines the necessary actions for preparedness, control and containment of Avian Influenza. The ICAR-National Institute of High Security Animal Diseases (NIHSAD), Bhopal, Madhya Pradesh, India, has been identified as the reference laboratory by the World organization for Animal Health (OIE). AI viruses are difficult to control because of the wildlife reservoir, the adaptability of the virus, and the lack of good control tools. Research efforts to increase the understanding of the virus biology and disease ecology are ongoing to develop newer and effective methods to control and eradicate the disease.

Keywords : *Avian influenza, water-birds, H5N1, Zoonosis.*

Introduction

Influenza

The deviation of man from the state in which he was originally placed by nature seems to have proved to him a prolific source of diseases.

- *Edward Jenner in "An Inquiry Into the Causes and Effects of the Variolae Vaccinae, Or Cow-Pox", 179*

How many of us would not have suffered from "flu"? In medical terms, flu is referred to as "influenza", an infectious disease caused by a virus. The causative organisms specifically are a group of orthomyxo-viruses (a family of RNA viruses), that spread through nasal secretions, faeces, blood and saliva. Recent World Health Organization (WHO) statistics indicate an annual global attack rate of 5-10% (in adults) and 20-30% (in children). Further, WHO also reports 3-5 million cases of severe illness resulting from influenza and about 2,50,000-5,00,000 deaths.

The orthomyxo-viruses causing influenza are classified into six genera, of which, three genera namely influenza virus-A, influenza virus-B and influenza virus-C are pathogenic (capable of causing disease) to humans. Each genus is further classified into a number of sub-types based on the surface protein configuration of the virus particle. The most commonly occurring sub-types are those belonging to the genera A and B, while C being relatively uncommon. In addition to humans, the influenza viruses also infect other hosts such as seals, horses, pigs, birds and dogs. The influenza-A virus is the only genus which infects both birds and humans, and is regarded as an important veterinary and human pathogen globally.

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Avian influenza

• A brief historical account

Detailed historical account on the origins of avian influenza are provided by Lupiani & Reddy and Swayne . The earliest report of fowl plague indicative of infections by the influenza virus in domestic poultry was reported by an Italian veterinarian and parasitologist Edoardo Bellarmino Perroncito (Figure 1) in 1878 in a paper titled *"epizoozia tifoide nei gallinacei"* [epizootic typhoid of fowl] . Eventual reports were sporadic, however, significant work focused on the isolation and study of the causative organism in the subsequent years (Table1). Until 1981, the disease was referred to as the 'fowl plague', which was then renamed as the Highly Pathogenic Avian Influenza (HPAI).

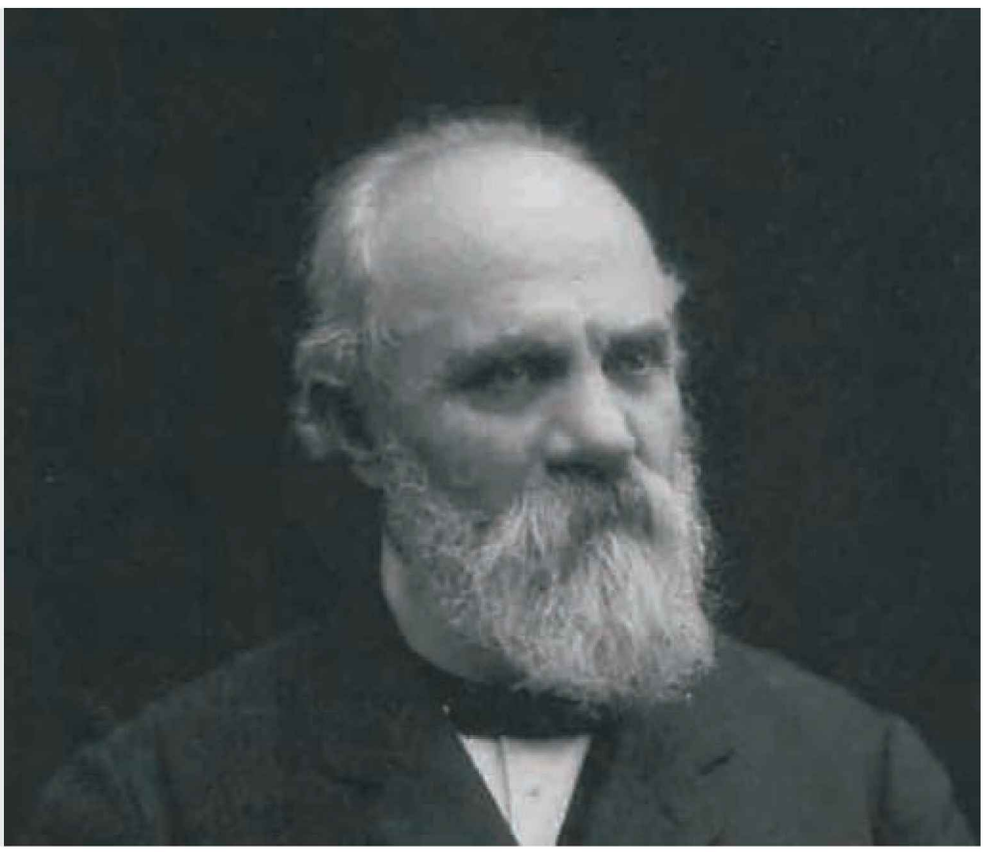

Figure 1 : *Edoardo Bellarmino Perroncito (1847–1936). Perroncito published the first paper describing the fowl plague in 1878,which is now known as the Highly Pathogenic Avian Influenza (HPAI).*

Table 1 : Chronological events in Avian Influenza Research [From (Lupiani & Reddy, 2009)]

Year	Event
1878	First description of highly pathogenic avian influenza (HPAI) or fowl plague
1880	Differentiation of HPAI from fowl cholera
1901	Identification of HPAI as a virus
1901-1930s	Major outbreaks of HPAI throughout the world
1918	Major human pandemic
1931	First influenza virus isolated (swine)
1941	Recognition of hemagglutination by influenza viruses
1942	HPAI and Newcastle disease virus shown to agglutinate red blood cells and to be different serologically
1955	HPAI virus shown to be a type A influenza virus
1959	Isolation of a HPAI virus serologically different from the classical fowl plague virus in hemagglutination inhibition test

1970s	Intensive sureillance of influenza viruses in wild birds and recognition that wild birds harbor all identified subtypes of influenza viruses
1971	Classification of influenza viruses based on antigenic properties of the NP (type) and HA and NA (subtype) proteins and the species of origin
1977-1981	Recognition that the presence of multiple basic amino acids in the HA cleavage site correlates with tissue spread and virulence of AI strains
1978	Recognition that the 1957(H2N2) and 1968 (HN) pandemic influenza viruses aroused by reassortment with AI viruses
1980	Classification of influenza viruses based on antigenic properties of the NP (type) and HA and NA (subtype) proteins regardless of the species of origin
1981	First International Symposium on Avian Influenza
1981	The name highly pathogenic avian influenza is proposed to substitute fowl plague
1999-2001	H9N2 virus transmission to humans
1997-present	HPAI H5N1 transmission to humans
2000s	H9N2 becomes endemic in Asia
2003-present	HPAI H5N1 spreads through Asia, Europe and Africa and becomes endemic in Asia

Definition

For statutory control purposes, the European Union defines Avian Influenza as:

'*an infection of poultry caused by either any influenza A virus that has an intravenous pathogenicity index in 6-week-old chickens greater than 1.2 or any influenza A virus of H5 or H7 subtype*' .

A much detailed definition adopted by the World Organization of Animal Health is:

'*… avian influenza in its notifiable form (NAI) is defined as an infection of poultry caused by any influenza A virus of the H5 or H7 subtypes or by any AI virus with an intravenous pathogenicity index (IVPI) greater than 1.2 (or as an alternative at least 75% mortality) as described below. NAI viruses can be divided into highly pathogenic notifiable avian influenza (HPNAI) and low pathogenicity notifiable avian influenza (LPNAI):HPNAI viruses have an IVPI in 6-week-old chickens greater than 1.2 or, as an alternative, cause at least 75% mortality in 4-to 8-week-old chickens infected intravenously. H5 and H7 viruses which do not have an IVPI of greater than 1.2 or cause less than 75% mortality in an intravenous lethality test should be sequenced to determine whether multiple basic amino acids are present at the cleavage site of the precursor haemagglutinin molecule (HA0); if the amino acid motif is similar to that observed for other HPNAI isolates, the isolate being tested should be considered as HPNAI. LPNAI are all influenza A viruses of H5 and H7 subtype that are not HPNAI viruses*'.

- **Avian influenza infections in birds**

Although the fowl plague was initially believed to be a distinctive disease to the poultry. It was only in the 1960's that the presence of avian influenza (AI) viruses was demonstrated in wild birds and was thought to circulate between wild and domestic birds (Dasen & Laver, 1970; Easterday, Trainer & Pereira, 1968; Winkler, Trainer, & Easterday, 1971; Zakstel; Skaja *et al.*, 1972). The first report of an AI virus from a wild bird was from a common tern *Sterna hirundo*. Since this discovery, AI viruses have been isolated from 105 wild bird species . AI infections have been reported in a range of hosts including wild birds, caged birds (pets), ratites (flightless birds), domestic poultry, chickens, turkeys, domestic ducks and other domestic poultry (pheasants, quails, fowl etc.). It has now been well documented that AI can spread from wild birds to domestic birds occasionally causing either low- or high-pathogenic outbreaks of AI .

The AI viruses are classified into Highly-pathogenic avian influenza (HPAI) [restricted to sub-types H5 and H7] and Low-pathogenecity avian influenza (LPAI), with the former having mortality rates closer to 100%. Infections resulting from LPAI strains produce mild disease symptoms including ruffled feathers, lessened activity, diarrhea, low food consumption and reduced egg production. LPAI strains upon infections often mutate to the HPAI strains leading to severe infections with highly mortality rates. All documented infections to date are caused by the H5 and H7 sub-types. The HPAI outbreaks recorded during 1959 – 2009 are presented in Table 2. A total of 28 outbreaks have been recorded during this period, and more than half of them occurred within the last ten years. In addition to risk of AI transforming into a pandemic, the huge economic losses incurred by nations suffering outbreaks are alarming.

Although AI viruses possibly can infect many species of wild birds, the general trend is indicative of infections mostly in species associated with aquatic habitats, specifically the avian orders Anseriformes (ducks, geese and swans) and

Table 2 : Major outbreaks of Highly Pathogenic Avian Influenza since 1959 [adopted from Alexander and Lupiani & Reddy].

S. No.	HPAI virus	Subtype	Species affected	Approximately number of birds culled
1	A/Chicken/Scotland/59	H5N1	Chicken	1 small farm
2	A/tem/South Africa/61	H5N3	Common tern	1300
3	A/turkey/England/63	H7N3	Turkey	29,000
4	A/turkey/Ontario/7732/66	H5N9	Turkey	8000
5	A/Chicken/Victoria/76	H7N7	Chickens, ducks	58,000
6	A/Chicken/Germany/79	H7N7	Chicken and goose	1 chicken and 1 goose farm
7	A/turkey/England/199/79	H7N7	Turkey	9000
8	A/Chicken/Pennsylvania/1370/83**	H5N2	Chicken turkey	17,000,000 chickens and turkeys
9	A/turkey/Ireland/1378/83	H5N8	Turkey	307,000 chickens, turkeys and mostly ducks
10	A/Chicken/Victoria/85	H7N7	Chickens	240,000
11	A/turkey/England/50-92/91	H5N1	Turkey	8000
12	A/Chicken/Victoria/1/92	H7N3	Chicken	18,000 broiler breeders, ducks
13	A/Chicken/Queenland/667-6/94	H7N3	Chickens	22,000
14	A/Chicken/Mexico/8623-607/94**	H5N2	Chicken	Millions?
15	A/turkey/Pakistan/447/94**	H7N3	Chicken	>6,000,000
16	A/Chicken/NSW/97	H7N4	Chicken	160,000 chickens, emus
17	A/Chicken/Hong Kong/97	H5N1	Chicken, duck	1,500,000 chickens and other domestic birds
18	A/Chicken/Italy330/97	H5N2	Chickens	8000 Chickens, turkeys, guinea-fowl, ducks, quail, pigeons, geese, pheasant
19	A/turkey/Italy/99**	H7N1	Turkey	14,000,000 chickens turkeys, guinea-fowl, ducks, quail, pheasant, ostriches
20	A/Chicken/Chile/02	H7N3	Chicken	700,000 chickens and turkeys
21	A/grey heron/Hong Kong/861.1/02	H5N1	Wild birds	Outbreak in wild birds; over 800,000 domestic birds were culled
22	A/Chicken/Netherlands/03**	H7N7	Chicken	>34,000,000
23	A/Chicken/Asia, Europe	H7N1	Chicken, duck	100s of millions and Africa/03-07**
24	A/Chicken/Texas/04	H5N2	Chicken	6600
25	A/Chicken/Canada/04**	H7N3	Chicken	16,000,000
26	A/ostrich/South Africa/04	H5N2	Ostrich	30,000
27	A/Chicken/North Korea/05	H7N7	Chicken	219,000
28	A/turkey/England/07	H5N1	Turkey	160,000

Footnote : ***Outbreaks with a larger spread leading to major economic losses.*

Charadriiformes (gulls, terns and shore-birds) . Such species make up nearly 60 percent of the wild birds infected with the H5N1 virus and also account for the greater proportion of wildlife mortalities (Figure.3).

• Avian influenza as a zoonotic disease

Of specific interest, in this context, is the fact that birds 'too' act as a host to the influenza virus. Humans 'interact' with birds in everyday life, and this provides the possibility that an infected bird could transmit disease to the human host. Evidently, this is possible only if the same pathogen can infect both the hosts and that the 'interactions' are such that they allow transmissions. This leads us to the domain of "zoonosis". Zoonoses (Greek: zoon-animal; nosos-ailment) are infectious diseases which are 'naturally transmissible' from animals to humans. The Centres for Disease Control and Prevention (CDC) report that nearly 75% of the Emerging Infectious Diseases (EID's refers to those infectious diseases which have rising incidences within the past 35 years) are of zoonotic (CDC, 2014). Given the extent of interactions between birds and humans, zoonotic diseases, especially of the avian origin, are a serious concern . Of specific zoonotic importance is the influenza virus-A sub-types H7N7, H5N1, H9N9, H7N3, H7N2 and H9N2.

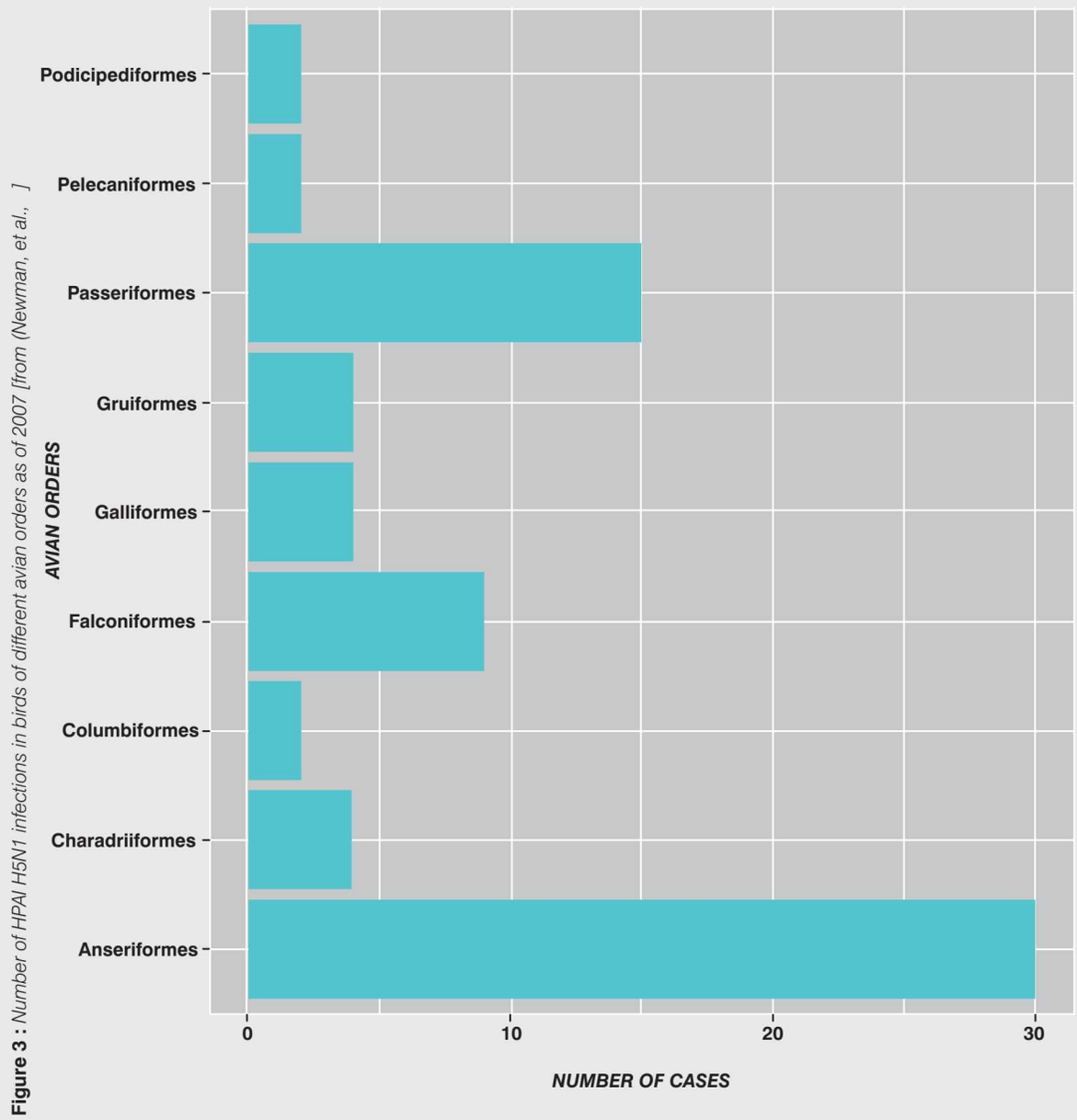

Figure 3 : *Number of HPAI H5N1 infections in birds of different avian orders as of 2007 [from (Newman, et al.,]*

The first report of avian flu in humans was documented in 1997 in Hong Kong during which 18 cases and six mortalities were registered. The WHO reports subsequent outbreaks and mortalities primarily in 15 countries, 2003 onwards. During 2003-2014, a cumulative total of 676 human infections were reported by 16 countries, of which 398 (57.88%) mortalities were recorded in 14 countries (Figure.2: WHO/GIP data as of December 4, 2014). The infection spreads to humans primarily through direct and/or close contact with sick and dead poultry. Although person-to-person transmission is claimed [see Ungchusak *et al.*], the CDC maintains that this is probably limited, inefficient and not sustained. However, the potential of such transmission is still being investigated. Symptoms in infected humans have ranged from conjunctivitis to 'influenza-like' illness (e.g. fever, sore throat, muscle pain) to respiratory illness. The highly pathogenic strain infections can be much severe and the said symptoms may be accompanied with multi-organ diseases and neurologic changes (e.g. seizures, altered mental status). Both type of infections might generally require hospitalization and a high risk of mortality is often associated with highly pathogenic strain infections. Diagnosis of the infection generally requires laboratory testing (molecular tests for the presence of the virus) of swabs from nose and/or throat of the

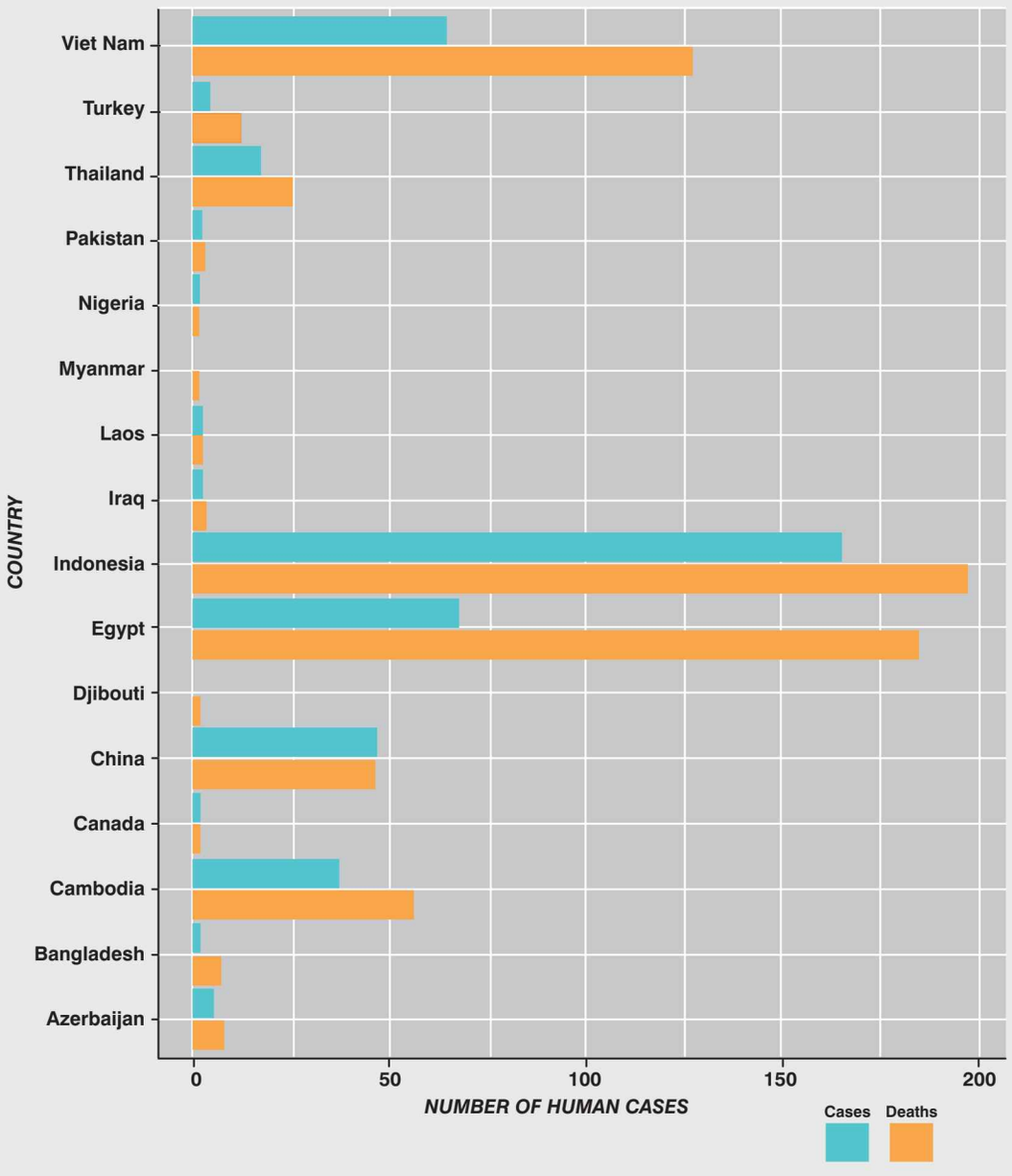

Figure 2 : *Country-wise cumulative number of confirmed human cases for avian influenza A (H5N1) reported to WHO, 2003-2014.*
Footnote : Source: *WHO/GIP, data in HQ as of December 4, 2014 (can be accessed online http://www.who.int/influenza/human_animal_interface/EN_GIP_20141223CumulativeNumberH5N1cases.pdf?ua=1)*

ill person in the initial days of the infection. Antiviral medications (oseltamivir and zananmivir) are advocated by the CDC and WHO for the treatment of human infections.

Monitoring Avian Influenza

Vaccines to protect birds from infections of specific sub-types of AI viruses have been developed and are used world-wide. Vaccination is usually a part of more comprehensive control programs to prevent AI outbreaks. A comprehensive control program usually involves the following components:

1. **Bio-security :** Movement controls of poultry, cleaning and disinfection of affected premises, limiting human access to affected premises and quarantining.
2. **Educating public about Avian Influenza :** Providing knowledge on how AI is transmitted and each individual's role in prevention, management or eradication.

3. **Diagnostics and Surveillance to detect the disease and infection :** Ability to detect the virus or evidence of infections in bird populations or their environment, or methods to verify freedom from such infections.
4. **Elimination of AI infected birds :** Removal of the infection source or susceptible sources to prevent continued environmental contamination and dissemination.
5. **Vaccination :** Decreasing host susceptibility; i.e., increasing host resistance to prevent infections or if infection occurs minimize the negative consequences.

Usage of these components in various combinations within a control strategy can prevent, manage, or eradicate AI. However, the use of AI vaccine alone can severely limit the effectiveness of any control strategy. Use of AI vaccine can manage the disease, but addition of the other four components of a comprehensive control program is needed to prevent or eradicate the disease and the infection.

The United Nations Environment Programme/Convention on Migratory Species (UNEP/CMS) and Food and Agriculture Organization (FAO) co-convened the Scientific Task Force on Avian Influenza and Wild Birds in 2005. The Scientific Task Force works as a communication and coordination network and continues to review the role of wild birds in the epidemiology of Avian Influenza and the impact of the disease on wild birds, promoting a balanced opinion based on currently available evidence. Task Force observers include the United Nations Environment Programme, World Health Organisation and World Organisation for Animal Health (OIE). Task Force members include FAO, CMS, and African Eurasian Waterbird Agreement, BirdLife International, Ecohealth Alliance, International Council for Game and Wildlife Conservation, Ramsar Convention, Royal Veterinary College, Wetlands International, and Wildfowl & Wetlands Trust.

Avian Influenza – Indian perspective

The first outbreak of avian influenza in India occurred in 2006. With 102 H5N1 outbreak reports between 2006 to current, India is in the list of the first fifteen countries world-wide with high AI incidence (Figure.4). The Ministry of Agriculture (Government of India) have prepared and circulated an Action Plan for the Preparedness, Control and Containment of Avian Influenza in 2012 (see Appendix-I). The plan details the necessary control measures and actions required to be taken in case an outbreak is detected. It also identifies key stake-holders at various levels. The ICAR-National Institute of High Security Animal Diseases (NIHSAD), Bhopal, Madhya Pradesh, India, has been identified as the a reference laboratory by the World organization for Animal Health (OIE). The OIE is the intergovernmental organisation responsible for improving animal health worldwide and has 180 member countries world-wide including India.

Conclusion

Since its first description as 'fowl plague' in 1878, avian influenza viruses have been well researched, highlighting its potential role in animal and public health. The role of avian influenza as an emerging infectious disease has also been highlighted by various agencies. It has often been referred to as a 'pandemic' owing to its nature of prevalence and the potential to be transmitted to humans. Close contact to sick and/or dead birds is necessary for the transmission of the disease to humans. Although a few sources claim person-to-person transmission, conclusive evidence to support this is lacking. As interactions between humans and birds are common, the prevalence of zoonotic disease, such as influenza remains high. Mitigation to prevent human transmission hence involves effective vaccination and eradication programs. Ongoing research is focussed on understanding the disease ecology and biological properties of the viruses.

Appendix-I : List of key references

Topic	Reference
Ramsar Wetland Disease Manual	(Cromie *et al.*, 2012) http://www.wwt.org.uk/conservation/saving-wetlands-and-wildlife/publications/ramsar-wetland-disease-manual/
Government of India, Action Plan for Preparedness, Control and Containment of Avian Influenza	http://dahd.nic.in/dahd/WriteReadData/Action%20Plan-Revised 30.07.12.pdf
History of Avian Influenza, Epidemiology, Disease risks, control measures and Policies	(Alexander, 2007; Swayne, 2009)
Overview of Avian Influenza	(Alexander, 2007; Cardona, et al., 2009)
Conventional and future diagnostics for avian influenza	(Charlton, *et al.*, 2009)
Avian influenza viruses in wild birds	(Olsen, *et al.*, 2006; Stallknecht, 2003)

Avian influenza field research and disease	(Capua & Alexander, 2009; Newman, Mundkur, & Harris, 2007) sampling manual
Avian influenza as a pandemic	(WHO, 2005)
Important websites	
World Health Organization	http://www.who.int/influenza/human_animal_interface/en/
World Organization for Animal Health	http://www.oie.int/en/animal-health-in-the-world/web-portal-on-avian-influenza/
World Animal Health Information Database	http://www.oie.int/wahis_2/public/wahid.php/Wahidhome/Home
ICAR-National Institute of High Security Animal Diseases	http://www.nihsad.nic.in/index.htm

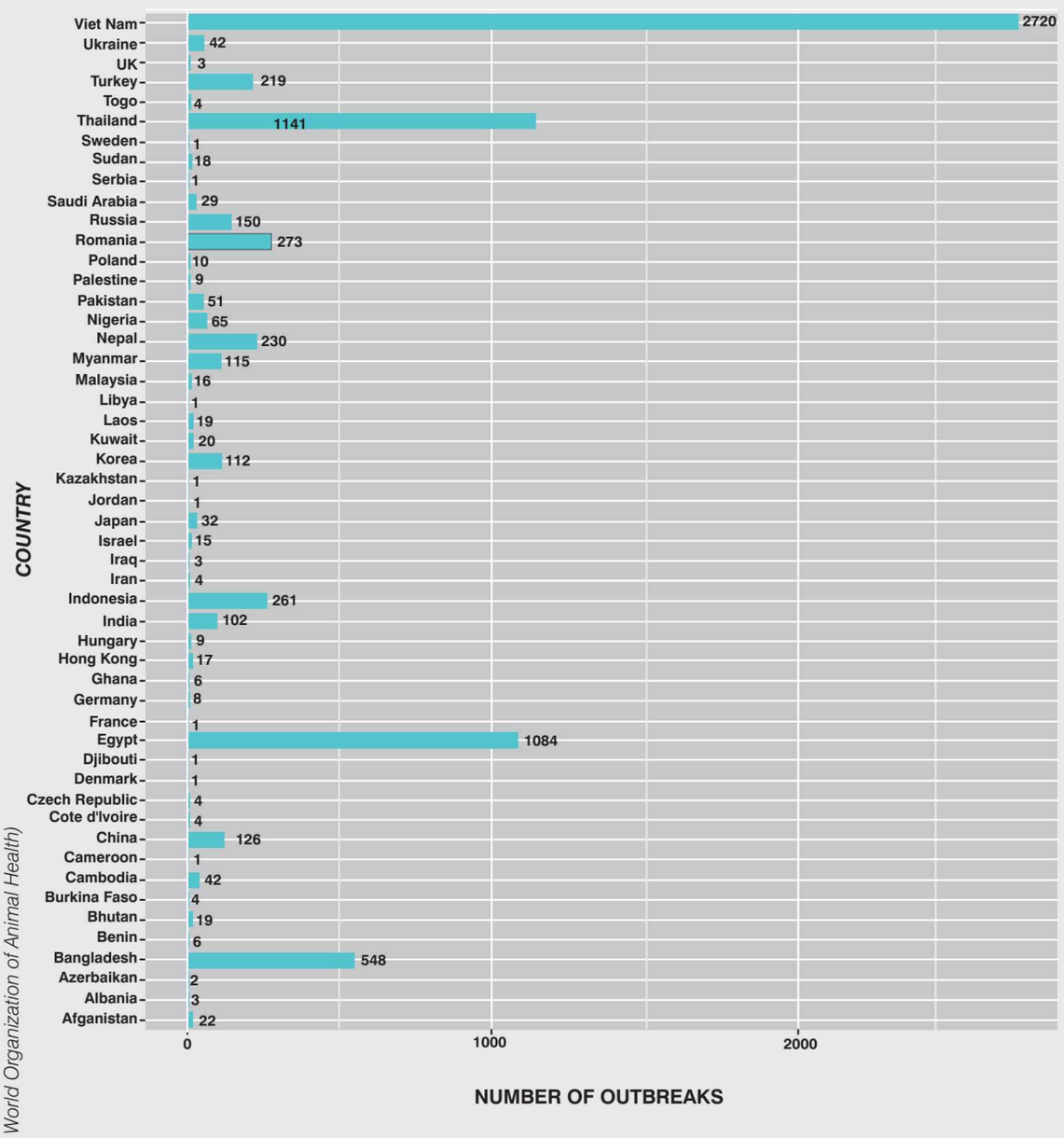

Figure 4 : *Country-wise details of H5N1 outbreaks in poultry during 2003-2014 (source Animal Health Information Department, World Organization of Animal Health)*

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