ISSN 1682-8356
ansinet.org/ijps

INTERNATIONAL JOURNAL OF

POULTRY SCIENCE

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308 Lasani Town, Sargodha Road, Faisalabad - Pakistan
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International Journal of Poultry Science 6 (10): 705-708, 2007
ISSN 1682-8356

Influenza A Viruses in Poultry: A Condensed Review

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Abstract: Influenza A viruses are comprised of 8 negative-sense RNA segments coding 11 proteins; divided into low and high pathogenicity. They use recombination, deletions and insertions to escape immune system detection. Its epidemiology is defined by interactions between the host, agent and environment. Wild birds are their natural reservoirs; they replicate in the intestinal tract, shed in faeces and transmitted by faecal-oral transmission. They attach to host cells by binding to sialosaccharides on the host cell surface, predominantly to type II pneumocytes, alveolar macrophages and nonciliated cuboidal epithelial cells in terminal bronchioles. High mortality rates of 61% in humans and 90-100% in poultry are seen.

Key words: Highly pathogenic avian influenza, HPAI H5N1, poultry, influenza A virus

Introduction

Influenza Viruses (IV) are orthomyxoviruses and are divided into A, B and C types. Influenza A Viruses (IAV) infect a wide range of domestic birds, wildfowl and shorebirds, but also many other species, including humans, pigs, horses, mink, felids and other mammals (Webster *et al*., 1992). Their genome is comprised of eight (8) negative-sense RNA segments that code for eleven (11) distinctive proteins. They are classified based on two surface glycoproteins expressed on virus particles: hemagglutinin (HA) and neuraminidase (NA). In poultry and wild birds, IAV representing 16 HA (H1-H16) and 9 NA (N1-N9) antigenic subtypes are in circulation (Fouchier *et al*., 2005; Webster *et al*., 1992) in numerous combinations (i.e. H_yN_x). The HA glycoprotein is initially synthesized as a single polypeptide (HA_n) that is cleaved into HA_1 and HA_2 subunits by cellular proteases; it mediates binding of the virus to host cells and fusion with endosomal membranes (Webster *et al*., 1992). The genes of H16 and H13 viruses are genetically distinct from IV from other hosts, suggesting they have been genetically isolated during sufficient time to invoke genetic differentiation (Fouchier *et al*., 2005).

During viral replication there is no control on fidelity and are therefore prone to many errors (Lamb and Choppin, 1983; Krystal *et al*., 1986; Webster *et al*., 2007). IAV have been isolated from avian species associated with captive birds in zoological collections (Ellis *et al*., 2004), wild birds imported for pet trade (Alexander, 2000) and with IAV-infected poultry flocks (Cross, 1987). IAV cleverly utilizes evolutionary strategies to escape detection by immune system cells and these include: classical recombination, deletion, insertion, re-assortment and mutation. It can use several of these strategies at any given time, for example, classical recombination (Pasick *et al*., 2005), deletion (Matrosovich *et al*., 1999) and insertion (Rott, 1980) have been detected in IAV from domestic poultry to mammals (Webster *et al*., 2007). This inherent capacity to mutate enables it to form novel viruses in other host species and to establish permanent viral lineages under exacting selective pressures.

Like most zoonotic diseases, the epidemiology of IAV in poultry is defined by interactions between hosts, agents and environments (Stallknecht and Brown, 2007). Among avian species IAV prevalence can vary greatly according to season and location and because individual species -and populations within species- exhibit different food, climatic and habitat preferences, migratory behaviours and agro-geographic ranges, individual species within these groups may play radically distinct but important roles in the epidemiology of bird flu (Webster *et al*., 2007).

Wild birds are the natural reservoirs of all IAV (Hinshaw *et al*., 1980; Suss *et al*., 1994), but most of them are asymptomatic; virus replicates predominantly in the intestinal tract (Slemons and Easterday, 1975; Fouchier *et al*., 2007), shed in faeces (Webster *et al*., 1978; Hinshaw *et al*., 1980) and subsequently transmitted and maintained by faecal-oral transmission (Hinshaw *et al*., 1979; Sandu and Hinshaw, 1981; Sinnecker *et al*., 1983), but poultry trade and mechanical movement of infected materials are also likely modes for spreading avian influenza (Alexander, 2000).

Relatively high virus prevalence in birds living in aquatic environments may in part be due to efficient transmission of faecal material via surface water (Webster *et al*., 1992). Other species in close proximity

to sick animals can get infected, including sea mammals, cats, dogs, minks and pigs, but these are usually transient and do not establish permanent lineages (Webster *et al*., 2007). IV in their natural setting show few amino acid changes, limited antigenic drift and have been described as being evolutionarily dormant (Gorman *et al*., 1992) thus hinting that under these unbothered conditions they are nearly perfectly adapted and that repeated mutations provide no selective advantage, therefore they are not favoured for further selection.

Naturally occurring infections of IAV are reported from free-living birds representing more than 90 species in 13 avian orders, mostly identified with the *Anatidae*, *Charadriidae* and *Scolopacidae* families (Stallknecht and Shane, 1988). All influenza A subtypes from H1 to H16 have been isolated from wild aquatic birds in Eurasia, whereas H14, H15 and H16 subtypes have not been detected in the Americas (Webster *et al*., 2007). IAV persistence in faeces (Beard *et al*., 1984; Lu *et al*., 2003), in allantoic fluid (Lu *et al*., 2003) and in nature varies from short-term to long-term, differing in their ability to remain infective depending on adaptations, water temperature, pH and salinity, within ranges that are normally encountered in surface water throughout the world (Stallknecht and Brown, 2007).

Salient Properties of Avian Influenza Viruses: Highly Pathogenic Avian Influenza (HPAI) emerges from Low Pathogenic (LP) viruses in host birds. IV show rapid evolution and this can occur in all gene segments but is most frequent in the HA and NA genes (Ludwig *et al*., 1995), where changes can result in antigenic drift (i.e. the process of random accumulation of mutations in viral genes). To date only H5 and H7 viruses have the capacity to become Highly Pathogenic (HP). The switch from a LP virus phenotype, common in wild birds and poultry, to the HP virus phenotype is achieved by the introduction of basic amino acid residues into the HA_n cleavage site, facilitating systemic virus replication due to enhanced HA cleavability outside the respiratory and intestinal tracts (Fouchier *et al*., 2007). Insertion of basic amino acids alone is not sufficient to make a virus HP, since this is a polygenic phenomenon involving multiple polymerase genes and other non-structural and matrix combinations, depending on the developing strain (Rott, 1980). These HP viruses mostly emerge in domestic poultry, but surprisingly, HP viruses are not perpetuated in aquatic birds because they are either stamped out or burned out.

HP viruses have differing levels of pathogenicity for gallinaceous poultry, however, molecular processes such as glycosylation in the vicinity of basic amino acids in the connecting peptides of the HA protein can mask high pathogenicity (Kawaoka and Webster, 1989).

Intermediate hosts: Interspecies transmission of IAV to other hosts, including mammals, is transitory and stable lineages are rarely established, however, this has changed with contemporary poultry industry production conditions. For example, H9N2, H6N2, H3N2 and H7N2 are now endemic in some parts of the world (Alexander, 2003).

A number of hosts, including dogs, cats, chicken, pig and quail have receptors for both avian and mammalian IV and have been proposed as intermediate hosts between wild birds and other mammals, including humans. Experimental infections in animals produce only a rapidly transient, low-level humoral immune response that may be sufficient to provide temporal protection against homologous re-infection, but unlikely to confer protection against heterologous re-infections (Kida *et al*., 1980).

Influenza viruses attach to host cells by binding of the HA to sialosaccharides on the host cell surface. Human influenza viruses prefer Sialic Acid (SA) α-2,6-Gal terminated saccharides, whereas avian influenza viruses prefer those terminating in SA α-2,3-Gal (Baigent and McCauley, 2003; Shinya *et al*., 2006). This preference explains direct transfers of IAV to humans and suggests that pigs may not be a required intermediate host; nevertheless, they could still serve to facilitate adaptation and continued transmissibility in animal and human populations.

Tissue and species specificity: In Lower Respiratory Tracts (LRT), H5N1 attaches predominantly to type II pneumocytes, alveolar macrophages and nonciliated cuboidal epithelial cells in terminal bronchioles. This predilection may contribute to the severity of pulmonary lesions. Type II pneumocytes are metabolically active and are the most numerous cell type lining the alveoli, thus selective targeting of these cells may lead to abundant virus production (van Riel *et al*., 2006).

Virus localization and replication deep in LRT limits the possibility for dispersion by aerosols through nasal discharge, coughing and/or sneezing. Recent studies suggest that HPAI viruses may become less pathogenic to ducks upon experimental infection, while retaining high pathogenicity for chickens (Hulse-Post *et al*., 2005; Sturm-Ramirez *et al*., 2004), thus allowing ducks (i.e. waterfowl) to be IAV silent carriers.

Discussion

Asian HPAI H5N1 virus is rapidly evolving. It has efficiently acquired environmental, geographical and host range attributes (Baigent and McCauley, 2003) to consider it a pandemic threat in poultry and a real potential exists (in Indonesia) for this virus to acquire consistent human-to-human transmissibility features. Furthermore, pets (i.e. cats) can be infected with H5N1 virus both by horizontal transmission and by feeding on

virus-infected birds (Kuiken *et al.*, 2004) and based on animal experiments, cats and ferrets are the most suitable animal models to study viral pneumonia on the basis of viral attachment pattern similarities (van Riel *et al.*, 2006).

High selective pressures appear as a major consequence of modern, intensive, industrial livestock production systems in that they potentially allow the rapid selection and amplification of pathogens of economic importance.

Species, geographical conditions and population structures are important in IAV maintenance, transmission and possibly long-distance movements. General poultry behaviour, spatial and temporal distribution, habitat utilization, migration patterns, population age structure and individual species susceptibility, among many other factors, need to be understood, or at least considered, when designing cost-effective surveillance strategies and evidence-based disease mitigation policies.

Concluding remarks

About two thirds of the world's poor are living in rural areas. Many of these people depend on livestock (i.e. poultry farming) for their livelihoods. It has become increasingly clear that production and local trade of high value agricultural goods, such as animal products, are motors for the economic development of these rural poor. Livestock diseases are consequentially detrimental to their livelihoods. Several livestock diseases, including highly pathogenic avian influenza and the strict health and sanitary requirements on major export markets, also exclude developing countries from participating in the vastly large and economically important global trade of animals and animal products. Through this condensed review that attempts to characterize influenza A viruses in poultry, it is our goal to disseminate knowledge about this zoonotic disease to all stakeholders with the ultimate intention of making better husbandry decisions, formulating appropriate livestock policies and reducing the impact of transmissible animal disease on smallholder livelihoods worldwide.

Acknowledgements

The authors are deeply grateful to Joachim Otte and John Cant for their sincere encouragement to publish poultry-related work and for facilitating a platform to freely exercise scientific thinking and creative expression.

Disclaimer[3]

Mr. Sigfrido Burgos is an international consultant at FAO. Ideas expressed in this article represent solely his personal opinions and views and are not necessarily endorsed by the international organization that currently employs him.

References

Alexander, D.J., 2000. A review of avian influenza in different bird species. Vet. Microbiol., 74: 3-13.

Alexander, D.J., 2003. Report on avian influenza in the eastern hemisphere during 1997-2002. Avian Dis., 47(suppl): 792-797.

Baigent, S.J. and J.W. McCauley, 2003. Influenza type A in humans, mammals and birds: Determinants of virus virulence, host-range and interspecies transmission. Bioessays, 25: 657-671.

Beard, C.W., M. Brugh and D. Johnson, 1984. Laboratory studies with the Pennsylvanian avian influenza virus (H5N2). Proceedings of the 88th annual conference of the United States Animal Health Association, pp: 462-473.

Cross, G.M., 1987. The status of avian influenza in poultry in Australia. Proceedings of the 2nd international symposium on avian influenza, Athens, Georgia, pp: 96-103.

Ellis, T.M., R.B. Bousfield, L.A. Bisset, K.C. Dyrting, G. Luk, S.T. Tsim, K. Sturm-Ramirez, R.G. Webster, Y. Guan and J.S. Peiris, 2004. Investigation of outbreaks of highly pathogenic H5N1 avian influenza in waterfowl and wild birds in Hong Kong in late 2002. Avian Pathol., 33: 492-505.

Fouchier, R., V. Munster, A. Wallensten, T.M. Bestebroer, S. Herfst, D.J. Smith, G.F. Rimmelzwaan, B. Olsen and A. Osterhaus, 2005. Characterization of a novel influenza A virus hemagglutinin subtype (H16) obtained from black-headed gulls. J. Virol., 79: 2814-2822.

Fouchier, R., V.J. Munster, J. Keawcharoen, A. Osterhaus and T. Kuiken, 2007. Virology of avian influenza in relation to wild birds. J. Wildlife Dis., 43: S7-S14.

Gorman, O., W. Bean and R. Webster, 1992. Evolutionary processes in influenza viruses: divergence, rapid evolution and stasis. Curr. Top. Microbiol. Immunol., 176: 75-97.

Hinshaw, V., R. Webster and B. Turner, 1979. Water-borne transmission of influenza A viruses. Intervirol., 11: 66-69.

Hinshaw, V., R. Webster and B. Turner, 1980. The perpetuation of orthomyxoviruses and paramyxoviruses in Canadian waterfowl. Canadian J. Microb., 26: 622-629.

Hulse-Post, D.J., K.M. Sturm-Ramirez, J. Humberd, P. Seiler, E.A. Govorkova, S. Krauss, C. Scholtissek, P. Puthavathana, C. Buranathai, T.D. Nguyen, H.T. Long, T.S. Naipospos, H. Chen, T.M. Ellis, Y. Guan, J.S. Peiris and R.G. Webster, 2005. Role of domestic ducks in the propagation and biological evolution of highly pathogenic H5N1 influenza viruses in Asia. Proc. Nat. Acad. Sci. USA, 102: 10682-7.

Kawaoka, Y. and R.G. Webster, 1989. Interplay between carbohydrate in the stalk and the length of the connecting peptide determines the cleavability of influenza virus hemagglutinin. J. Virol., 63: 3296-3300.

Kida, H., R. Yanagawa and Y. Matsuoka, 1980. Duck influenza lacking evidence of disease signs and immune response. Infect. Immun., 30: 547-553.

Krystal, M., R. Li, D. Lyles, G. Pavlakis and P. Palese, 1986. Expression of three influenza virus polymerase proteins in a single cell allows growth complementation of viral mutants. Proc. Nat. Acad. Sci. USA, 83: 2709-2713.

Kuiken, T., G. Rimmelzwaan, D. van Riel, G. van Amerongen, M. Baars, R. Fouchier and A. Osterhaus, 2004. Avian H5N1 influenza in cats. Sci., 306: 241.

Lamb, R.A. and P.W. Choppin, 1983. The gene structure and replication of influenza virus. Ann. Rev. Biochem., 52: 467-506.

Lu, H., A.E. Castro, K. Pennick, J. Liu, Q. Yang, P. Dunn, D. Weinstock and D. Henzler, 2003. Survival of avian influenza virus H7N2 in SPF chickens and their environments. Avian Dis., 47: 1015-1021.

Ludwig, S., L. Stitz, O. Planz, H. Van, W.M. Fitch and C. Scholtissek, 1995. European swine virus as a possible source for the next influenza pandemic. Virol., 212: 555-561.

Matrosovich, M., N. Zhou, Y. Kawaoka and R. Webster, 1999. The surface glycoproteins of H5 influenza viruses isolated from humans, chickens and wild aquatic birds have distinguishable properties. J. Virol., 73: 1146-1155.

Pasick, J., K. Handel, J. Robinson, J. Copps, D. Ridd, K. Hills, H. Kehler, C. Cottam-Birt, J. Neufeld, Y. Berhane and S. Czub, 2005. Intersegmental recombination between the haemagglutinin and matrix genes was responsible for the emergence of a highly pathogenic H7N3 avian influenza virus in British Columbia. J. Gen. Virol., 86: 727-731.

Rott, R., 1980. Genetic determinants for infectivity and pathogenicity of influenza viruses. Philos. Trans. Royal Soc. London, Series B, Biol. Sci., 288: 393-399.

Sandu, T. and V.S. Hinshaw, 1981. Influenza A virus infection in domestic ducks. In Proceedings of the first international symposium on avian influenza, R.A. Bankowski (Ed.). Carter Composition Corporation, Richmond, Virginia, pp: 222-227.

Shinya, K., M. Ebina, S. Yamada, M. Ono, N. Kasai and Y. Kawaoka, 2006. Avian flu: Influenza virus receptors in the human airway. Nature, 440: 435-436.

Sinnecker, R., H. Sinnecker, E. Zilske and D. Kohler, 1983. Surveillance of pelagic birds for influenza A viruses. Acta Virol., 27: 75-79.

Slemons, R.D. and B.C. Easterday, 1975. The natural history of type A influenza viruses in wild waterfowl. In Third international wildlife disease conference, L.A. Page (Ed.). Plenum Press, New York, New York, pp: 215-224.

Stallknecht, D. and J.D. Brown, 2007. Wild birds and the epidemiology of avian influenza. J. Wildlife Dis., 43: S15-S20.

Stallknecht, D. and S. Shane, 1988. Host range of avian influenza virus in free-living birds. Vet. Res. Comm., 12: 125-141.

Sturm-Ramirez, K., T. Ellis, B. Bousfield, L. Bissett, K. Dyrting, J.E. Rehg, L. Poon, Y. Guan, M. Peiris and R.G. Webster, 2004. Re-emerging H5N1 influenza viruses in Hong Kong in 2002 are highly pathogenic to ducks. J. Virol., 78: 4892-4901.

Suss, J., J. Schafer, H. Sinnecker and R. Webster, 1994. Influenza virus subtypes in aquatic birds of eastern Germany. Arch. Virol., 135: 101-114.

van Riel, D., V. Munster, E. de Wit, G. Rimmelzwaan, R. Fouchier, A. Osterhaus and T. Kuiken, 2006. H5N1 virus attachment to lower respiratory tract. Sci., 312: 399.

Webster, R.G., M. Yakhno, V.S. Hinshaw, W.R. Bean and K.G. Murti, 1978. Intestinal influenza: Replication and characterization of influenza viruses in ducks. Virol., 84: 268-278.

Webster, R.G., W.J. Bean, O.T. Gorman, T.M. Chambers and Y. Kawaoka, 1992. Evolution and ecology of influenza A viruses. Microbiol. Rev., 56: 152-179.

Webster, R., S. Krauss, D. Hulse-Post and K. Sturm-Ramirez, 2007. Evolution of influenza A viruses in wild birds. J. Wildlife Dis., 43: S1-S6.