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Reports of Avian Influenza H5N1 in Cats and Dogs

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Abstract: Avian Influenza virus (H5N1 subtype) interspecies transmission capability is a characteristic feature that has attracted worldwide attention as a potential risk to human health. Pet carnivores (cats and dogs) are susceptible to infection, shed virus, can remain asymptomatic and thus can be silent disease carriers. These potential intermediate hosts are commonly kept as pets in rural and urban households and therefore could serve as vehicles for viral disease spread to children and adults.

Key words: Avian Influenza, HPAI, bird flu, fowl plague, H5N1, cats, dogs

Introduction

Avian Influenza (AI) virus of the H5N1 subtype has crossed the species barrier and it has infected a wide range of domestic birds, wildfowl and shorebirds, but also many other species, including humans, pigs, dogs, horses, mink, cats and other mammals (Fouchier *et al*., 2007; Mehrabanpour *et al*., 2007; Webster *et al*., 1992). Cats experimentally infected with AI H5N1 are susceptible to infection and shed virus (Kuiken *et al*., 2004) and reports of positive testing and virus isolation in dogs in Thailand have surfaced (Butler, 2006; Songserm *et al*., 2006). Currently, consistent human-to-human transmissibility is not yet a salient feature of AI H5N1, but a real potential exists for this virus to rapidly develop it under strong selective pressures. Therefore, pet carnivores infected with AI H5N1 may pose a threat to human health.

Influenza viruses attach to host cells by binding of the hemagglutinin surface glycoprotein 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; Matrosovich *et al*., 1999; Shinya *et al*., 2006).

In humans, AI H5N1 attaches predominantly to type II pneumocytes and nonciliated cuboidal epithelial cells in terminal bronchioles of Lower Respiratory Tracts (LRT). This predilection may contribute to the severity of pulmonary tissue 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 prolific virus production. Virus attachment to cat LRT is similar to that in human tissues (van Riel *et al*., 2006).

Avian influenza in cats: Anecdotal reports of cat deaths near poultry outbreaks in SE Asia (ProMed, 2004) prompted a Dutch research team to experimentally inoculate domestic cats intratracheally with AI H5N1 from a fatal human case in Vietnam and found that cats did get clinically sick, shed virus, transmitted disease horizontally to other cats and subsequently died (Kuiken *et al*., 2004). Moreover, follow-up studies revealed that infected cats excrete virus in their faeces as well as in coughed-out droplets, suggesting aerial disease transmission as a novel route (Rimmelzwaan *et al*., 2006).

Phylogenetic mapping of hemagglutinin gene reveals two separate lineages: clade 1 and 2. Vietnamese feline cases are reportedly caused by AI H5N1 clade 1 (Amonsin *et al*., 2006) and only one cat infected with clade 2 virus (Yingst *et al*., 2006), which might have caused deaths of Thai tigers and leopards (Keawcharoen *et al*., 2004).

During 2005, in the Suphan Buri district of rural Thailand, 111 cats were tested for antibodies against H5N1 and 8 cats were found positive (7.21%) by national investigators (Butler, 2006). Months later, in early 2006, three German cats were reportedly infected naturally with AI H5N1 virus A/swan/Germany/R65/06, in which partial nucleotide sequencing of hemagglutinin revealed it was genetically related to a dead swan (*Cygnus cygnus*) found in Northern Germany (Klopfleisch *et al*., 2007).

These results clearly demonstrate successful productive infections in cats, clinically evidenced by fever, lethargy, lymphoid necrosis in spleen, prostration, necrosis of the adrenal cortex, eyelid protrusion, conjunctivitis, laboured breathing, bronchointerstitial pneumonia, marked random hepatic necrosis and diffused alveolar damage. Infection can occur both by feeding on AI virus-infected birds and by horizontal transmission. For more detailed descriptions of pathology and signs in cats, see Thiry *et al*. (2007).

Avian influenza in dogs: As briefly described above, felids, including wild cats and tigers, are now known

influenza virus carriers, but dogs where not suspected to be susceptible until early 2004, when equine-originated influenza virus (H3N8) infection of greyhound dogs was first reported in Florida, USA (Crawford *et al*., 2005).

Complementarily, Butler (2006) reports that a team of researchers in the city of Bangkok working at the National Institute of Animal Health tested 629 village dogs in central Thailand and found that 160 dogs (25.44%) tested positive for antibodies against H5N1. Furthermore, virologists at Chulalongkorn University were able to isolate the virus from one dog in a follow-up study.

Beagles are susceptible to AI H5N1 infection and can shed virus nasally without signs of disease. Viral attachment occurs in receptors located in the LRT, trachea and nose (Maas *et al*., 2007). Similarly to dogs infected with H3N8, the course of infection of specific pathogen-free dogs with H5N1 resulted in asymptomatic seroconversion with varying degrees of virus excretion/shedding (Crawford *et al*., 2005; Maas *et al*., 2007).

Songserm *et al*. (2006) describes in detail necropsy and histopathological findings from a dead 1-yr old dog submitted for veterinary examination after having ingested a HPAI H5N1-infected duck during a 2004 outbreak in Thailand. Generally speaking, successfully productive infections in canines can be diagnosed and compared to necropsy findings that include, among others, pulmonary oedema, severe bronchio-alveolar congestion, bloody nasal discharge, as well as congestion of the liver, kidney and spleen. Moreover, histopathological slides exhibit interstitial pneumonia with inflammatory cell infiltration, haemolysis with black-brownish particles found in pulmonary parenchyma, hepatic focal necrosis, mild renal nephritis with tubular degeneration and pulmonary oedema. Genetic comparisons indicate that this canine isolate was similar to a HPAI virus collected from a tiger in Thailand during mid-2004.

Concluding remarks: Considering that repeated, reliable, scientifically-valid diagnoses of successful HPAI H5N1 infections of cats and dogs have been found in SE Asia; we believe that feline and canine contacts with poultry and wild birds should be avoided or intentionally restricted in avian influenza outbreak areas/regions as to prevent possible transmission between these species. Opportunistic feeding of cats and dogs on AI H5N1-infected birds/poultry could facilitate yet another opportunity for this virus to adapt to mammals, thereby increasing the risks of a global human influenza pandemic and thus an unforeseen public health chaos of catastrophic proportions.

Urban veterinary professionals-seeing these animals on an almost daily basis-should be advised about this potential risk and also recommended to avoid direct contact with infected cats and dogs by wearing masks, gloves and protective goggles. Also, owners of infected pets should be instructed to minimize contact with these animals, as they are vectors of AI disease.

Epidemiologically speaking, mice and ferrets are also susceptible to AI H5N1 and nowadays are increasingly often kept as small domestic companion pets; therefore, they should also be included in surveillance lists endorsed by international animal health organizations and ministries of animal and public health.

Pet to human transmission potential warrants further studies. These animals need now to be considered and included in animal monitoring programs during HPAI H5N1 outbreaks in the future. Also, funding should be earmarked by research institutes, universities and governments to conduct more research into transmission dynamics.

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Disclaimer[3]

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