

University of Nebraska - Lincoln

DigitalCommons@University of Nebraska - Lincoln

USDA National Wildlife Research Center - Staff
Publications

U.S. Department of Agriculture: Animal and Plant
Health Inspection Service

2019

What Are the Transmission Mechanisms of Influenza A Viruses in Wild Mammals?

J. Jeffrey Root

National Wildlife Research Center, jeff.root@aphis.usda.gov

Follow this and additional works at: https://digitalcommons.unl.edu/icwdm_usdanwrc

 Part of the [Natural Resources and Conservation Commons](#), [Natural Resources Management and Policy Commons](#), [Other Environmental Sciences Commons](#), [Other Veterinary Medicine Commons](#), [Population Biology Commons](#), [Terrestrial and Aquatic Ecology Commons](#), [Veterinary Infectious Diseases Commons](#), [Veterinary Microbiology and Immunobiology Commons](#), [Veterinary Preventive Medicine, Epidemiology, and Public Health Commons](#), and the [Zoology Commons](#)

Root, J. Jeffrey, "What Are the Transmission Mechanisms of Influenza A Viruses in Wild Mammals?" (2019). *USDA National Wildlife Research Center - Staff Publications*. 2257.

https://digitalcommons.unl.edu/icwdm_usdanwrc/2257

This Article is brought to you for free and open access by the U.S. Department of Agriculture: Animal and Plant Health Inspection Service at DigitalCommons@University of Nebraska - Lincoln. It has been accepted for inclusion in USDA National Wildlife Research Center - Staff Publications by an authorized administrator of DigitalCommons@University of Nebraska - Lincoln.

What Are the Transmission Mechanisms of Influenza A Viruses in Wild Mammals?

J. Jeffrey Root

US Department of Agriculture, National Wildlife Research Center, Fort Collins, Colorado

Some influenza A viruses (IAVs) represent serious potential threats to public and agricultural health, with 3 notable examples from the past decade. During 2009, a novel H1N1 IAV (A[H1N1]pdm09), which was first detected in the United States, spread rapidly throughout many regions of the world [1]. In the United States alone, the Centers for Disease Control and Prevention estimated that >60 million human cases were associated with this emergent and pandemic virus [1]. During 2013, a novel H7N9 avian-origin IAV (Asian lineage avian influenza A[H7N9] virus) was first detected in China. This virus not only cost the poultry industry more than \$1 billion through culling and market closures, it also proved to be detrimental to public health, as this virus is readily transmitted to humans and can cause moderate-to-high rates of mortality [2, 3]. More recently, a highly pathogenic clade 2.3.4.4 avian IAV was first detected in North America during 2014. Ultimately, the introduction of this virus (and subsequent reassortant viruses) elicited the most expensive highly pathogenic IAV outbreak in US history [4], with total losses estimated to be billions of dollars [5]. These 3 examples exemplify the

enormous burdens that some IAVs can place on public and agricultural health systems and suggest that a diversity of studies need to be conducted to address the complex epidemiology of these virus-host systems.

The majority of isolations of avian IAVs in wild birds have been associated with the avian orders Anseriformes (eg, ducks, geese, and swans) and Charadriiformes (eg, gulls, terns, and shorebirds), and certain species in the former are thought to be key reservoirs of avian IAVs [6]. Indeed, aquatic birds are likely the reservoir hosts of all avian IAVs, and the fecal-oral route of transmission is thought to be the primary mechanism of viral spread among this diverse group of birds [7].

Distinct lineages of IAVs have also become established in select nonhuman mammals. For example, multiple IAV lineages are established in swine and equine populations [8]. While these established mammalian IAV lineages are readily transmitted among conspecifics [8, 9], IAV transmission within wild mammalian species without established lineages has not been well studied, and little evidence suggests that these viruses are maintained within these species in natural settings. However, mammalian species that do not maintain IAVs within their populations could still play a role in key transmission events.

Several IAV experimental infection studies have been conducted with wild mammals. While some species have been shown to shed low or moderate amounts of virus (eg, raccoons [*Procyon lotor*] [10, 11]), others have been shown to shed high levels of virus (eg, striped skunks

[*Mephitis mephitis*] and cottontail rabbits [*Sylvilagus* species] [12, 13]). Many mammalian experimental infection studies have been conducted using avian IAVs without prior mammalian adaptation, thereby suggesting that several wild mammalian species are susceptible to avian IAVs under laboratory conditions. Of significance, at least 1 wild mammalian species is susceptible to low doses of virus inoculum [14], which may be a crucial attribute when considering naturally acquired infections.

During recent years, evidence of IAV natural exposures has been reported for a number of wild mammalian species. Some recent examples from a long list of diverse candidates include antibody detections in raccoons in the United States and Japan [10, 15], antibody and viral detections in plateau pika (*Ochotona curzoniae*) in China [16–18], and antibody detections in water deer (*Hydropotes inermis*) and a leopard cat (*Prionailurus bengalensis*) in Korea [19]. Although these mammals clearly appear to have been exposed to various IAVs, the mechanism by which they were exposed and their potential to transmit IAVs remains largely undetermined.

It has been suggested that raccoons may come into contact with IAVs in the aquatic environments in which they can often be found, and habitats that concentrate raccoons and waterfowl (eg, areas with limited riparian habitat) may increase exposure and subsequent antibody prevalence estimates [10]. Similarly, researchers have suggested that plateau pika may be exposed through IAV-laden secretions of waterfowl deposited within

Received 14 January 2019; editorial decision 14 January 2019; accepted 28 January 2019; published online March 6, 2019.

Correspondence: J. Jeffrey Root, PhD, US Department of Agriculture, National Wildlife Research Center, 4101 La Porte Avenue, Fort Collins, CO (Jeff.Root@aphis.usda.gov).

The Journal of Infectious Diseases® 2019;XX(XX):0–0

Published by Oxford University Press for the Infectious Diseases Society of America 2019. This work is written by (a) US Government employee(s) and is in the public domain in the US. DOI: 10.1093/infdis/jiz033

shared foraging sites [16]. Water deer were hypothesized to have been exposed to IAVs through their peridomestic tendencies and/or potential interactions with waterfowl or shared habitats [19]. The documented leopard cat exposure adds an additional species to an expanding list of IAV exposures in felids [19], some of which are thought to have been exposed through ingestion of virus-laden bird carcasses [20].

Some experimental work addressing possible IAV transmission routes to mammals has been conducted. In a study addressing 3 ecological routes of IAV transmission to raccoons, results indicated that transmission of a low-pathogenic virus subtype occurred through ingestion of virus-contaminated water but was not successful through the consumption of virus-contaminated eggs and avian carcasses [11]. In contrast, highly pathogenic IAV H5N1-infected bird carcasses represented a successful vehicle to transmit this IAV subtype to red fox (*Vulpes vulpes*) [21]. Furthermore, anecdotal evidence from zoo-housed and wild carnivores indicates that virus-contaminated carcasses may have the capacity to infect some species within this taxonomic group with some subtypes [20, 22].

Overall, there appear to be 3 predominant hypotheses for wild mammal exposure to avian IAVs in natural settings. These include shared habitat with waterfowl [10, 16], shared water sources with waterfowl [10, 11], and predation/scavenging upon waterfowl [10, 11, 21]. In this issue of *The Journal of Infectious Diseases*, a unique analysis was used to address whether host phylogenetic relatedness, sociality, and/or diet have an influence on IAV antibody prevalence and subtype diversity in an understudied set of wild African mammals from a region of Africa where information on IAV epidemiology is scant [23]. Thus, the analyses presented that are associated with diet, especially as it relates to diet of carnivorous and/or scavenging mammals that commonly feed on

birds, build on one of the 3 hypotheses mentioned above.

In their analyses, Soilemetzidou et al [23] reported that neither phylogenetic relatedness (ie, the recency of a common ancestor shared by 2 species) nor gregariousness (ie, the tendency of a species to form social groups) of the mammalian species analyzed significantly influenced IAV antibody frequency or the diversity of subtypes detected within a species; however, a higher seroprevalence and a greater number of IAV subtypes were noted in carnivorous species that are thought to regularly feed on avian species. This analysis supports previous experimental work that showed productive infections in mammalian carnivores fed highly pathogenic IAV-infected bird carcasses [21]. Further, the diversity of IAV subtypes reported, including those that are not H5 nor H7 [23], suggests that mammalian antibody responses associated with low-pathogenic IAVs may more commonly occur through consumption of virus-laden bird carcasses than previous experimental work has suggested [11].

Although IAV antibody detections in wild mammals, especially those presumed to be from avian sources, is of scientific interest, several items must be taken into consideration before any implications associated with the epidemiological impacts of these exposures can be realized. First, various mammalian species could be readily exposed to IAVs through various mechanisms (eg, virus-infected bird carcasses), as determined by antibodies, but not have the capacity to shed the viruses at sufficient levels to initiate transmission to a population of interest. Second, IAV antibodies in social mammals could represent a common exposure through environmental contamination and not necessarily the ability to transmit the virus among conspecifics. Third, certain behavioral traits, such as peridomestic tendencies that put an animal into close contact with humans or domestic poultry, could be an important facet of the actual risk that a given

mammalian species poses to agricultural or zoonotic infections. Thus, when possible/practical, experimental infection studies addressing transmission to, from, and within a species would be valuable to complement results found in serosurveys. This type of information, coupled with knowledge of key behavioral traits, will help to elucidate the role a given wild mammalian species might play in the transmission and maintenance of IAVs.

Notes

Financial support. This work was supported by the US Department of Agriculture.

Potential conflicts of interest. Author certifies no potential conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

- Centers for Disease Control and Prevention. Past pandemics. <https://www.cdc.gov/flu/pandemic-resources/basics/past-pandemics.html>. Accessed 6 December 2018.
- Liu J, Xiao H, Wu Y, et al. H7N9: a low pathogenic avian influenza A virus infecting humans. *Curr Opin Virol* **2014**; 5:91–7.
- Liu S, Sun J, Cai J, et al. Epidemiological, clinical and viral characteristics of fatal cases of human avian influenza A (H7N9) virus in Zhejiang Province, China. *J Infect* **2013**; 67:595–605.
- Spackman E, Pantin-Jackwood MJ, Kapczynski DR, Swayne DE, Suarez DL. H5N2 highly pathogenic avian influenza viruses from the US 2014–2015 outbreak have an unusually long pre-clinical period in turkeys. *BMC Vet Res* **2016**; 12:260.
- Greene JL. Update on the highly-pathogenic avian influenza outbreak of 2014–2015. *Congressional Research Service* **2015**; R44114. <https://fas.org/sgp/crs/misc/R44114.pdf>. Accessed 6 December 2018.

6. Stallknecht DE, Shane SM. Host range of avian influenza virus in free-living birds. *Vet Res Commun* **1988**; 12:125–41.
7. Webster RG. Influenza virus: transmission between species and relevance to emergence of the next human pandemic. *Arch Virol Suppl* **1997**; 13:105–13.
8. Reperant LA, Rimmelzwaan GF, Kuiken T. Avian influenza viruses in mammals. *Rev Sci Tech* **2009**; 28:137–59.
9. OIE. Swine influenza. http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/SWINE_INFLUENZA.pdf. Accessed 10 December 2018.
10. Hall JS, Bentler KT, Landolt G, et al. Influenza infection in wild raccoons. *Emerg Infect Dis* **2008**; 14:1842–8.
11. Root JJ, Bentler KT, Shriner SA, et al. Ecological routes of avian influenza virus transmission to a common mesopredator: an experimental evaluation of alternatives. *PLoS One* **2014**; 9:e102964.
12. Root JJ, Shriner SA, Bentler KT, et al. Shedding of a low pathogenic avian influenza virus in a common synanthropic mammal - the cottontail rabbit. *PLoS One* **2014**; 9:e103513.
13. Root JJ, Shriner SA, Bentler KT, et al. Extended viral shedding of a low pathogenic avian influenza virus by striped skunks (*Mephitis mephitis*). *PLoS One* **2014**; 9:e70639.
14. Root JJ, Shriner SA, Ellis JW, VanDalen KK, Sullivan HJ. Low viral doses are sufficient to infect cottontail rabbits with avian influenza A virus. *Arch Virol* **2017**; 162:3381–8.
15. Yamaguchi E, Sashika M, Fujii K, et al. Prevalence of multiple subtypes of influenza A virus in Japanese wild raccoons. *Virus Res* **2014**; 189:8–13.
16. Zhou J, Sun W, Wang J, et al. Characterization of the H5N1 highly pathogenic avian influenza virus derived from wild pikas in China. *J Virol* **2009**; 83:8957–64.
17. Su S, Xing G, Wang J, et al. Characterization of H7N2 avian influenza virus in Wild Birds and Pikas in Qinghai-Tibet plateau area. *Sci Rep* **2016**; 6:30974.
18. Yan Y, Gu JY, Yuan ZC, et al. Genetic characterization of H9N2 avian influenza virus in plateau pikas in the Qinghai lake region of China. *Arch Virol* **2017**; 162:1025–9.
19. Kim HK, Kim HJ, Noh JY, et al. Serological evidence of H5-subtype influenza A virus infection in indigenous avian and mammalian species in Korea. *Arch Virol* **2018**; 163:649–57.
20. Keawcharoen J, Oraveerakul K, Kuiken T, et al. Avian influenza H5N1 in tigers and leopards. *Emerg Infect Dis* **2004**; 10:2189–91.
21. Reperant LA, van Amerongen G, van de Bildt MW, et al. Highly pathogenic avian influenza virus (H5N1) infection in red foxes fed infected bird carcasses. *Emerg Infect Dis* **2008**; 14:1835–41.
22. Klopfleisch R, Wolf PU, Wolf C, et al. Encephalitis in a stone marten (*Martes foina*) after natural infection with highly pathogenic avian influenza virus subtype H5N1. *J Comp Pathol* **2007**; 137:155–9.
23. Soilemetzidou E-S, de Bruin E, Franz M, et al. Diet may drive influenza A virus exposure in African mammals. *J Infec Dis* **2019**; In press.