2018

Lessons learned from research and surveillance directed at highly pathogenic influenza A viruses in wild birds inhabiting North America

Andrew M. Ramey
US Geological Survey, aramey@usgs.gov

Thomas J. DeLiberto
U.S. Department of Agriculture, Thomas.J.DeLibertot@aphis.usda.gov

Yohannes Berhane
National Centre for Foreign Animal Disease, yohannes.berhane@inspection.gc.ca

David E. Swayne
Southeast Poultry Research Laboratory, david.swayne@ars.usda.gov

David E. Stallknecht
University of Georgia, dstall@uga.edu

Virology 518 (2018) 55–63

Contents lists available at ScienceDirect

Virology

journal homepage: www.elsevier.com/locate/virology

Lessons learned from research and surveillance directed at highly pathogenic influenza A viruses in wild birds inhabiting North America

Andrew M. Ramey[a,*], Thomas J. DeLiberto[b], Yohannes Berhane[c,d], David E. Swayne[e], David E. Stallknecht[f]

[a] US Geological Survey, Alaska Science Center, 4210 University Drive, Anchorage, AK 99508, USA
[b] National Wildlife Disease Program, Wildlife Services, Animal and Plant Health Inspection Service, US Department of Agriculture, Fort Collins, CO 80521, USA
[c] Canadian Food Inspection Agency, National Centre for Foreign Animal Disease, Winnipeg, Manitoba, Canada R3E 3M4
[d] Department of Animal Science, University of Manitoba, Winnipeg, Canada
[e] Exotic and Emerging Avian Viral Diseases Research Unit, Southeast Poultry Research Laboratory, U.S. National Poultry Research Center, Agricultural Research Service, U.S. Department of Agriculture, Athens, GA, USA
[f] Southeastern Cooperative Wildlife Disease Study, Department of Population Health, College of Veterinary Medicine, University of Georgia, Athens, GA 30602, USA

ARTICLE INFO

Keywords:
Clade 2.3.4.4
H5
Highly pathogenic
Influenza A
North America
Research
Surveillance
Wild bird

ABSTRACT

Following detections of highly pathogenic (HP) influenza A viruses (IAVs) in wild birds inhabiting East Asia after the turn of the millennium, the intensity of sampling of wild birds for IAVs increased throughout much of North America. The objectives for many research and surveillance efforts were directed towards detecting Eurasian origin HP IAVs and understanding the potential of such viruses to be maintained and dispersed by wild birds. In this review, we highlight five important lessons learned from research and surveillance directed at HP IAVs in wild birds inhabiting North America: (1) Wild birds may disperse IAVs between North America and adjacent regions via migration, (2) HP IAVs can be introduced to wild birds in North America, (3) HP IAVs may cross the wild bird-poultry interface in North America, (4) The probability of encountering and detecting a specific virus may be low, and (5) Population immunity of wild birds may influence HP IAV outbreaks in North America. We review empirical support derived from research and surveillance efforts for each lesson learned and, furthermore, identify implications for future surveillance efforts, biosecurity, and population health. We conclude our review by identifying five additional areas in which we think future mechanistic research relative to IAVs in wild birds in North America are likely to lead to other important lessons learned in the years ahead.

1. Introduction

The importance of wild birds as a reservoir for influenza A viruses (IAVs) has been recognized since the 1960s (Easterday et al., 1968), in part, through research and surveillance efforts targeting wild birds in North America (defined in this review as Canada and the United States of America; USA). However, the nature of research and surveillance efforts directed towards IAVs in wild birds in North America has evolved considerably over the past 50 years, and particularly, since the repeated detection of highly pathogenic (HP) IAVs of Goose/Guangdong (Gs/GD) lineage in wild birds inhabiting Asia, Europe, and Africa beginning shortly after the start of the new millennium. In 2002, an outbreak of H5N1 Gs/GD lineage HP IAV in a zoological collection and sympatric free-ranging birds in Hong Kong marked the first mortality of wild aquatic birds attributed to a HP IAV since 1961 (Ellis et al., 2004; Sturm-Ramirez et al., 2004). A subsequent outbreak of H5N1 HP IAV in wild birds at Qinghai Lake, China in 2005 (Chen et al., 2005) raised concerns about the role of migratory birds in the dispersal of Gs/GD lineage HP IAVs, including the potential for the introduction of such viruses into North America via intercontinental migratory bird movements. Thus, following detections of HP IAVs in wild birds inhabiting East Asia after the turn of the millennium, the intensity of sampling of wild birds for IAVs increased throughout much of North America and the objectives for many research and surveillance efforts were directed towards detecting foreign origin HP IAVs and understanding the potential of such viruses to be maintained and dispersed by wild birds. In this review, we highlight five important lessons we feel have been learned from research and surveillance directed at HP IAVs in wild birds inhabiting North America.

* Corresponding author.
E-mail address: aramey@usgs.gov (A.M. Ramey).

https://doi.org/10.1016/j.virol.2018.02.002
Received 15 November 2017; Received in revised form 29 January 2018; Accepted 2 February 2018
0042-6822/ Published by Elsevier Inc.

1.1. Wild birds may disperse IAVs between North America and adjacent regions via migration

Following the 2005 outbreak of H5N1 HP IAV at Qinghai Lake, China, considerable research was conducted in North America to assess the evidence for dispersal of IAVs by wild birds between East Asia and North America via Alaska, a pathway by which large numbers of waterbirds make interhemispheric migratory movements (Winker and Gibson, 2010). Although previous research efforts had not identified an entirely foreign-origin IAV genomic constellation in North America (including Alaska; Winker et al., 2007), and Eurasian lineage gene segments had been found to be relatively rare in IAV isolates derived from samples collected in Alberta, Canada and Delaware Bay, USA (Krauss et al., 2007), the infrequent detection of Eurasian lineage gene segments in IAVs isolated from wild birds sampled in North America suggested at least low levels of intercontinental viral dispersal via Alaska or another unidentified pathway. Thus, a series of targeted investigations were conducted to assess the dispersal of IAVs between East Asia and North America via Alaska where the East Asian-Austral Asian, Central Pacific, and Pacific Americas flyways overlap.

Through the genetic characterization of IAVs derived from northern pintails (*Anas acuta*) sampled in Alaska during a single year, Koehler et al. (2008) found evidence for a higher proportion of isolates with Eurasian lineage gene segments as compared to previous reports for waterfowl sampled at Alberta, Canada (Krauss et al., 2007). Follow-up studies confirmed this observation (Ramey et al., 2010a) and, furthermore, provided support for the dilution by distance of Eurasian lineage gene segments within North America (Pearce et al., 2009; Ramey et al., 2010a, 2010b). That is, sampling of waterbirds in western Alaska, near the Asian-North American interface, has consistently provided a high probability of encounter of Eurasian lineage gene segments as compared to elsewhere in North America, which supports this region as a probable location for viral introductions via migratory birds (Ramey et al., 2010a, 2010b, 2011; Reeves et al., 2013). Indeed, through additional sampling of wild birds in western Alaska in 2011, H9N2 IAVs were isolated from swabs collected from a northern pintail duck and an emperor goose (*Chen canagica*), two waterfowl species with intercontinental migratory tendencies (Miller et al., 2005; Hupp et al., 2007, 2011), that shared > 99% genomic identity to viruses previously identified in wild birds inhabiting China and South Korea (Ramey et al., 2015). Furthermore, IAVs sharing similarly high genetic identity to these H9N2 viruses detected in wild birds sampled in Alaska, China, and South Korea have not been identified in domestic poultry and the South Korean H9N2 strain, A/bean goose/Korea/220/2011, did not replicate in experimentally inoculated three week-old chickens (Lee et al., 2016a), providing further evidence that this genomic constellation was most likely dispersed intercontinentally by wild birds.

In November 2014, a clade 2.3.4.4 HP IAV of the H5N8 subtype comprised of eight Eurasian lineage gene segments was detected in the Pacific Americas Flyway of North America and it was widely speculated that this HP IAV was dispersed between East Asia and North America by wild birds (Lee et al., 2015; Verhagen et al., 2015; Lycett et al., 2016). While the introduction of a clade 2.3.4.4 IAV from East Asia to North America via Alaska is consistent with: (1) previous evidence for viral dispersal via this pathway, (2) intercontinental migratory pathways of wild birds, (3) the timing of arrival for migrants from Alaska to the region where clade 2.3.4.4 IAVs were first detected in North America (Hill et al., 2017), and (4) proposed evolutionary pathways of reassortant clade 2.3.4.4 HP IAVs in wild birds in the Pacific Northwest of the USA and Canada (Lee et al., 2016b; Ramey et al., 2016a, 2017; Hill et al., 2017), definitive support for the hypothesis that migratory birds introduced H5N8 clade 2.3.4.4 HP IAV into North America from East Asia remains elusive. None-the-less, it is reasonable to conclude that the circulation of economically costly poultry pathogens or IAVs of concern to public health in wild birds inhabiting East Asia poses some degree of risk to the biosecurity of Canada and the USA.

In addition to targeted investigations in Alaska to assess evidence for the intercontinental exchange of IAVs between North America and East Asia, research efforts conducted since 2005 have also examined the potential for wild birds to disperse viruses between North America and adjacent regions via other migratory routes identified through ornithological investigations. For example, research conducted in Newfoundland, Canada has provided evidence that seabirds, including gulls (*Larus* spp.) and murres (*Uria* spp.), may facilitate the exchange of viruses between Western Europe and North America via a trans-North Atlantic pathway (Wille et al., 2011; Huang et al., 2014a, 2014b). This includes the purported first detection of a wholly Eurasian lineage virus in North America (Huang et al., 2014a). Additionally, research conducted in Texas and Louisiana (USA), Barbados, Guatemala, and Columbia, collectively provide support for the hypothesis that Neotropical migrants, such as blue-winged teal (*Anas discors*), may disperse IAVs among locations in North America, Central America, the Caribbean Islands, and northern South America (Douglas et al., 2007; González-Reiche et al., 2012; Karlsson et al., 2013; Ramey et al., 2016b). Thus, surveillance for the early detection of foreign-origin IAVs in wild birds inhabiting North America may be optimized by targeted sampling at geographical regions where genetic data for IAVs and ornithological information collectively support an increased probability for viral introductions into the USA and Canada from adjacent regions.

1.2. HP IAVs can be introduced to wild birds in North America

The first confirmed outbreak of HP influenza A in North American birds per the current Office International des Epizooties (OIE) definition (i.e., characterized by a polybasic hemagglutinin [HA] cleavage site), affected domestic poultry in Ontario, Canada in 1966 (Swayne, 2008; Ping et al., 2012). Subsequent outbreaks of HP IAVs in North America during the period of 1983–2014 affected domestic gallinaceous birds in Pennsylvania, Maryland, New Jersey, and Virginia, USA in 1983 (Buisch et al., 1984); Texas, USA in 2004 (Lee et al., 2005; Pelzel et al., 2006); British Columbia, Canada in 2004 (Hirst et al., 2004); and Saskatchewan, Canada in 2007 (Berhane et al., 2009). In each of these outbreaks, it also appears that a low pathogenic (LP) IAV precursor circulated, at least briefly, among domestic gallinaceous birds before developing high pathogenicity in poultry (Suarez and Senne, 2000; Lee et al., 2005; Pasick et al., 2005; Berhane et al., 2009; Ping et al., 2012). No poultry-adapted LP IAVs epidemiologically connected to HP outbreaks or HP IAVs causing disease in domestic poultry were detected in wild birds in North America prior to 2014. Thus, prior to autumn 2014, there was no evidence for spill-over of HP IAVs into wild birds inhabiting the USA or Canada, or even for the re-introduction of LP IAVs into the wild bird reservoir following poultry adaptation.

In late November 2014, increased mortality was observed among domestic turkeys and chickens in British Columbia, Canada leading to the identification of a HP IAV of the H5N2 subtype (Pasick et al., 2015). Through genetic sequencing, this HP H5N2 IAV was identified as an intercontinental reassortant virus descended from the H5 Gs/GD lineage clade 2.3.4.4 HP IAVs that were concurrently circulating in Eurasia and one or more IAVs circulating among waterfowl inhabiting North America (Pasick et al., 2015). In early December 2014, H5N2 and H5N8 clade 2.3.4.4 HP IAVs were isolated from samples collected from a wild northern pintail (*Anas acuta*) and a captive-reared gyrfalcon (*Falco rusticolus*) that had recently fed upon a wild American wigeon (*Anas americana*), respectively, in Washington, USA (Ip et al., 2015). The H5N2 clade 2.3.4.4 HP isolates recovered from poultry in British Columbia, Canada and a wild northern pintail in Washington, USA were genomically highly similar (i.e., > 99% shared nucleotide identity), closely related to HP IAVs circulating in East Asia at the HA gene, and the apparent product of reassortment between a clade 2.3.4.4 HP IAV and one or more IAVs circulating in North America (Ip et al., 2015). In contrast, the H5N8 clade 2.3.4.4 HP IAV isolated from a captive-reared gyrfalcon was genomically highly similar (i.e., > 99% shared

nucleotide identify at all gene segments) to HP IAVs associated with outbreaks in East Asia (Ip et al., 2015). Thus, initial genetic evidence supported the introduction of H5 Gs/GD lineage HP IAVs from East Asia into North America prior to late November 2014 and reassortment with IAVs that were circulating among wild birds. As such, the genetic lineage of the HA gene segment for these viruses was designated as intercontinental group A (icA; Lee et al., 2015).

Following the initial detection of H5 clade 2.3.4.4 HP IAVs in British Columbia, Canada and Washington, USA in November–December 2014, additional detections of HP H5N2 and H5N8 IAVs with similar genome constellations were identified in domestic poultry in these locations, as well as numerous additional states throughout the USA including: Oregon, California, Montana, North Dakota, South Dakota, Nebraska, Kansas, Minnesota, Iowa, Missouri, Arkansas, and Wisconsin (Jhung et al., 2015; Lee et al., 2016b; Hill et al., 2017; Ramey et al., 2017; United States Department of Agriculture (USDA), 2017a). Concurrently, similar genomic constellations of HP H5N2 and H5N8 IAVs were detected in American wigeon, northern pintail, and numerous additional species of wild waterfowl and raptors including American green-winged teal (*Anas crecca*), Canada goose (*Branta canadensis*), mallard (*Anas playrhynchos*), northern shoveler (*Anas clypeata*), wood duck (*Aix sponsa*), bald eagle (*Haliaeetus leucocephalus*), Cooper's hawk (*Accipiter cooperii*), peregrine falcon (*Falco peregrinus*), and snowy owl (*Bubo scandiacus*) sampled through active and passive surveillance in British Columbia, Washington, Oregon, Idaho, Nevada, Utah, Kansas, Minnesota, and Wisconsin (OIE, 2015; Lee et al., 2016b; Hill et al., 2017; Ramey et al., 2017; USDA, 2017a). Furthermore, novel reassortant clade 2.3.4.4 HP IAV genome constellations of the H5N1 and H5N8 subtypes were detected in wild waterfowl in Washington (Torchetti et al., 2015), Oregon (Lee et al., 2016b), and California (Ramey et al., 2017). In the case of reassortant H5N1 clade 2.3.4.4 HP IAV, a genomically similar constellation was also identified in a backyard poultry flock in British Columbia, Canada (Berhane et al., 2016), although the isolate recovered had a 19 amino acid deletion in the neuraminidase (NA) stalk indicating poultry adaptation of this particular virus. In all of these instances, the best available evidence at the time of manuscript preparation suggests that reassortant Gs/GD lineage clade 2.3.4.4 HP IAVs detected in North America during 2014–2015 were formed through evolutionary pathways that included IAVs maintained in wild birds (Lee et al., 2016b; Ramey et al., 2016a, 2017; Hill et al., 2017).

The estimated prevalence of clade 2.3.4.4 HP IAVs in wild bird samples collected in the Pacific Americas Flyway during December 2014–February 2015 was estimated to be 0.8–1.3% using real-time reverse transcriptase PCR in two studies (Bevins et al., 2016; Ramey et al., 2017) or 1.4% across the USA during December 2014–June 2015 outbreak period as calculated using unpublished surveillance data collected by the USDA (99 HP clade 2.3.4.4 IAV positives/7085 total samples; USDA, 2017b). Clade 2.3.4.4 HP IAVs were detected in wild birds in the Pacific, Central, and Mississippi flyways of North America during the outbreak period, but not the Atlantic Flyway. Prevalence estimates during the December 2014–June 2015 outbreak period were biased by targeted active surveillance in the western USA following initial detection of clade 2.3.4.4 HP IAVs during the waterfowl hunting season, a combination of active and passive surveillance efforts in some data summaries, and reduced active surveillance in wild birds inhabiting North America during February–June 2015 following the closure of waterfowl hunting seasons in many areas.

It is estimated that clade 2.3.4.4 icA HP IAVs affected approximately 50.4 million domestic birds in 21 states in the USA during December 2014–June 2015 (Swayne et al., 2017; USDA, 2017a). Subsequent to the last detections of clade 2.3.4.4 HP IAVs in domestic poultry in North America in June 2015, there were four additional purported detections of clade 2.3.4.4 HP IAVs in wild birds using molecular techniques as of the time of manuscript preparation (USDA, 2017b). However, only a single detection of H5N2 clade 2.3.4.4 HP IAV derived from a sample collected from a mallard in Alaska during August 2016 has been genomically characterized and published (Lee et al., 2017a). Thus, as no genomically highly similar reassortant H5 clade 2.3.4.4 icA HP IAVs have been detected outside of North America, it appears that such viruses persisted in either an unidentified biotic or abiotic reservoir in North America for at least an additional year following the well-described outbreak in Canada and the USA. The current status of H5 clade 2.3.4.4 HP IAVs in North America is unknown. It is plausible that such viruses have been extirpated in Canada and the USA through management practices applied to domestic poultry and via population immunity of wild birds, and that any further outbreaks of clade 2.3.4.4 HP IAVs in North America would require another introduction event. Notably, Gs/GD lineage clade 2.3.4.4 group B (H5N6 and H5N8) and group C (H5N6) IAVs have spread throughout Asia during 2016–2017 causing outbreaks in poultry and infections with mortality in wild birds (Lee et al., 2017c), and could therefore represent future biological threats to North American poultry production systems via introduction by intercontinental migrants.

During the December 2014–June 2015 outbreak period in North America, clade 2.3.4.4 icA HP IAVs were detected from samples collected from both apparently healthy and diseased wild birds. Samples testing positive for clade 2.3.4.4 HP IAVs that were collected from dabbling ducks were predominately derived from apparently healthy birds (i.e., those not displaying overt clinical signs of disease) at the time of harvest/sampling (Torchetti et al., 2015; Bevins et al., 2016; Ramey et al., 2017; USDA, 2017a,b) or birds associated with disease attributed to another cause (Ip et al., 2015). In contrast, a high proportion of detections of H5 clade 2.3.4.4 HP IAVs in North American raptors (including a captive individual) and geese were derived from samples originating from sick or deceased animals (Ip et al., 2015; Bevins et al., 2016; USDA, 2017a,b). Sampling biases may have impacted these results, however, as dabbling ducks were disproportionally sampled during active surveillance programs whereas raptors and geese were largely sampled via passive surveillance.

The 2014–2015 outbreak of clade 2.3.4.4 HP IAVs in North America represents the first detections of HP IAVs in wild birds in North America and provides additional evidence that some viruses of the Gs/GD lineage may be well-adapted to waterfowl as has been supported through experimental challenge studies (DeJesus et al., 2016; Pantin-Jackwood et al., 2016). It should be noted that there still is not any evidence that the HP IAV phenotype is selected for or can evolve in wild birds in North America or elsewhere. H5 clade 2.3.4.4 icA HP IAVs were clearly introduced into wild and domestic birds in North America after already having evolved a HP phenotype, presumably in domestic poultry in East Asia (Hu et al., 2015). Furthermore, more recent outbreaks of HP IAVs in North American poultry in 2016 and 2017 are consistent with the premise that the HP IAV phenotype emerges in domestic gallinaceous poultry (Killian et al., 2016; Xu et al., 2017; USDA, 2017c) and that prompt containment efforts prevent spill-over into wild birds and limit viral spread.

1.3. HP IAVs may cross the wild bird-poultry interface in North America

With a single exception, all documented outbreaks of HP IAVs in North America appear to be the product of LP IAVs being introduced into domestic poultry production systems where they developed high pathogenicity and were subsequently eradicated through containment and depopulation efforts (Suarez and Senne, 2000; Lee et al., 2005; Pasick et al., 2005; Berhane et al., 2009; Xu et al., 2017). However, during the 2014–2015 outbreak of HP clade 2.3.4.4 IAVs in North America, it appears that there were numerous instances of spill-over of HP viruses across the wild bird-poultry interface in the USA and Canada through unidentified mechanisms. Support for the transmission of HP IAVs between wild and domestic birds is provided through the detection of highly similar genomic constellations of HP IAVs in both wild and domestic birds (Pasick et al., 2015; Ip et al., 2015; Berhane et al., 2016), inferred phylogenetic relationships among viral genomes

recovered from sampling of infected poultry farms and through wild bird surveillance suggestive of spill-over events (Lee et al., 2016b; Grear et al., 2017a; Hill et al., 2017; Ramey et al., 2017), and analysis of epidemiological data suggestive of indirect contact between wild and domestic birds (Xu et al., 2016). While transmission of HP IAVs across the wild bird-poultry interface is not unprecedented from a global perspective, particularly for Gs/GD lineage IAVs, the apparent spread of HP IAVs between wild and domestic birds in the USA and Canada during 2014–2015 (via either direct or indirect routes) suggests that biosecurity practices in place in North America at that time were not sufficient to prevent economically costly IAVs that were circulating in wild birds from entering poultry production systems, even once such pathogens had been identified through national and international wild bird surveillance programs.

The apparent first instances of spill-over of HP IAVs between wild and domestic birds in North America may be, at least partially, a function of increased infectivity of HP clade 2.3.4.4 IAVs for waterfowl and gallinaceous poultry at medium to high exposure doses as compared to other HP viruses. Laboratory challenge studies lend support to this hypothesis and may be attributed to the evolution of Gs/GD lineage HP IAVs through serial infections in both gallinaceous poultry and domestic waterfowl over more than two decades (Perkins et al., 2003; Hulse-Post et al., 2005; Pantin-Jackwood et al., 2016). However, a recent laboratory study also found that numerous other HP IAVs associated with previous gallinaceous poultry outbreaks were infectious in mallards at 10^6 mean embryo infectious doses via intranasal challenge, replicated in various tissues to relatively high titers, were shed via both the oropharynx and the cloaca, and caused few clinical signs in this species (Pantin-Jackwood et al., 2016). This research further supports the premise that introduction of HP IAVs from poultry to wild waterfowl is biologically possible, but that insufficient or non-sustained exposure of wild birds may prevent infection. Thus, enhanced biosecurity and containment of HP IAV outbreaks in poultry may be important in preventing spill-over of HP IAVs to North American wild birds and limiting virus spread.

1.4. The probability of encountering and detecting a specific virus may be low

Following the 2005 outbreaks of Gs/GD lineage H5N1 HP IAV in Qinghai Lake, China, national surveillance efforts were conducted in the USA and Canada to detect the possible introduction of this virus into North America via migratory birds. However, it was and remains unknown at what prevalence H5N1 HP IAVs were circulating in wild birds in East Asia that share migratory connectivity with North America, how many individuals comprised the affected population, and how additional epidemiological considerations (e.g., length of prepatent period; duration, route, and consistency of viral shedding; etc.) affected the probability of detection. Thus, surveillance programs were developed without rigorous estimates for probabilities of encounter (likelihood of sampling an infected bird within a population) or detection (likelihood of identifying an infected bird given sampling and diagnostic limitations).

Despite extensive active surveillance efforts in both the USA and Canada, the H5N1 Gs/GD lineage HP IAV that led to the 2005 Qinghai Lake outbreak has not been detected in wild (or domestic) birds in North America. However, the detection of other IAVs in wild birds, including Gs/GD lineage clade 2.3.4.4 HP IAVs in 2014–2015, provides important insight into effectiveness of active surveillance programs and suggests that the probability of encountering and detecting a specific virus may be extremely low, at least for viruses that circulate at relatively low prevalence within a population. For example, in 2010, H14 subtype IAVs were detected in wild birds in North America for the first time (Nolting et al., 2012). Viruses of the H14 subtype had not been detected since 1982 when they were recovered from samples collected from waterfowl and gulls in the former Soviet Union (Kawaoka et al., 1990). The lack of detection of H14 IAVs in global surveillance efforts during 1982–2010 suggests that such viruses may be relatively rare in the wild bird reservoir. Since initial detection in waterfowl in North America in 2010, a total of only eleven detections of H14 IAVs have been reported in the USA through July 2017 (Boyce et al., 2013; Fries et al., 2014; Ramey et al., 2014a, 2016c) with reports of viruses originating from samples collected during 2010–2015. Furthermore, during this period, it appears that H14 subtype IAVs were dispersed by wild birds across North America and to the northern Neotropics where they had been repeatedly detected in blue-winged teal during 2011–2013 (Ramey et al., 2014a; Gonzalez-Reiche et al., 2016). Thus, the best available evidence suggests that H14 subtype IAVs may have been introduced from Eurasia to North America (Fries et al., 2013), subsequently dispersed across the continent to the Neotropics (Ramey et al., 2014b), circulated among wild birds in North America for at least six years (Ramey et al., 2016c), while having only been reported in the USA eleven times despite ongoing research and surveillance efforts. While there are numerous confounding variables relative to methodological differences among surveillance efforts which make calculations of encounter and detection probabilities complicated for this particular example, the implication of relatively few detections of H14 IAVs among the many thousands of samples screened in the USA during this same time period is clear. IAVs may be maintained in the wild bird reservoir at relatively low levels that may require extensive sampling effort to encounter and detect.

Surveillance efforts conducted during and subsequent to the 2014–2015 outbreak of clade 2.3.4.4 HP IAVs in North America present another example of how the encounter and detection probabilities for specific IAVs may be low. For example, the best available data suggest that H5 clade 2.3.4.4 HP IAVs were introduced into North America from East Asia via migratory birds, yet such viruses were not detected in Alaska during the late summer and autumn migration period of 2014 despite the collection of more than a thousand samples from wild birds inhabiting western and southcentral regions of the state (Ramey et al., 2016a; Hill et al., 2017). During December 2014–February 2015, which may have been the epidemiological peak of infection of wild birds with clade 2.3.4.4 HP IAVs in the Pacific Americas Flyway, such IAVs were identified in only 0.8–1.3% of samples collected (Bevins et al., 2016; Ramey et al., 2017) despite sampling efforts having been informed through passive surveillance (i.e., mortality events) and periodic detections in domestic birds. Detection of clade 2.3.4.4 HP IAVs was markedly lower at other areas of North America during this period and following the outbreak (Krauss et al., 2016; Ramey et al., 2016d, 2017).

Subsequent to the apparent eradication of Gs/GD HP IAV from North American poultry in June 2015, there have been only four purported detections of clade 2.3.4.4 HP IAVs in wild birds using molecular techniques during the period of July 2015–June 2017 despite the collection and testing of more than 80,000 samples in the USA (USDA, 2017b). Thus, it is plausible that such viruses have circulated within a very large population of North American waterfowl at extremely low prevalence making the probability of encounter and detection exceedingly small. It is possible that an unsampled or abiotic reservoir facilitated the maintenance and subsequent infrequent detection of clade 2.3.4.4 IAVs in wild birds during the July 2015–June 2017 post-outbreak period, or that putative icA positive samples (as identified through rRT-PCR) for which sequence data were not recovered represent false-positive detections. However, evidence for substantial genetic drift between the H5N2 clade 2.3.4.4 HP IAV recovered from a mallard sampled in Alaska in August 2016 as compared to the most closely related isolates recovered in North America during the 2014–2015 outbreak period (Lee et al., 2017a) suggests that these explanations may be unlikely. Thus, low probability of encountering and detecting clade 2.3.4.4 IAVs in a large population of waterfowl in North America during July 2015–June 2017 appears to be a more plausible explanation for infrequent detection during this period as compared to other possible scenarios.

1.5. Population immunity of wild birds may influence HP IAV outbreaks in North America

The observation that juvenile wild birds are more likely to be infected with IAVs as compared to adults was recognized in early investigations of IAV ecology in North America and is widely accepted as being a function of the high concentration of immunologically naïve birds at breeding/staging areas in late summer and early autumn prior to migration (Hinshaw et al., 1980). Thus, immunologic responses of wild birds to IAVs have long been recognized as fundamentally important to viral ecology. However, more recent studies provide insight as to how population immunity could influence HP IAV outbreaks in North America. For clarity, there is still no evidence that the HP IAV phenotype is selected for or can evolve in wild birds in North America. Thus potential influences of population immunity of wild birds relative to HP IAV outbreak dynamics in North America are limited to the maintenance of H5 and H7 subtype LP IAVs (i.e., those with the potential to develop high pathogenicity in poultry after introduction into production systems) and/or the maintenance and dispersal of HP IAVs introduced into wild birds in North America as occurred during the 2014–2015 outbreak.

Surveillance for IAVs in wild birds suggests that the relative prevalence of viruses of particular HA subtypes may be seasonal in North America (Ramey et al., 2014a; USDA, 2017b) and concurrent laboratory challenge studies provide insight into host factors that may drive such trends. For example, recent laboratory challenge studies provide evidence that homo- and heterosubtypic immunity to specific HA subtypes, as acquired through prior IAV infection in waterfowl, may influence infection dynamics among IAVs of different HA subtypes. That is, prior infection with IAVs may provide partial or complete immunity (as measured through metrics of infectivity such as duration and magnitude of viral shedding) to waterfowl for viruses of the same HA subtype, and likewise, partial or complete protective immunity against IAVs of different HA subtypes (Costa et al., 2010; Jourdain et al., 2010; Pepin et al., 2012; Latorre-Margalef et al., 2017; Segovia et al., 2017). While complete protective immunity precludes subsequent infection altogether, partial protective immunity may influence the duration of infection, viral shedding patterns, and total viral load of infected individuals that had been previously exposed to IAVs (Costa et al., 2010; Jourdain et al., 2010; Pepin et al., 2012; Latorre-Margalef et al., 2017; Segovia et al., 2017). The level of homo- and heterosubtypic HA immunity conferred to a bird previously exposed to IAV is likely influenced by the genetic similarity of the antigenic determinants of IAV strains to which a bird is exposed (Latorre-Margalef et al., 2017; Segovia et al., 2017). Thus, the population immunity of wild birds in North America may influence the space and time at which H5 and H7 subtype LP IAVs may be most prevalent in the population and therefore the relative risk of introduction into poultry production systems where there is spatiotemporal overlap.

Additionally, population immunity may influence the introduction and perpetuation of HP IAV infections in wild birds upon exposure from foreign sources or via contact with infected domestic birds. For example, laboratory challenge studies provide evidence that prior infection with LP IAVs may influence homo- and heterosubtypic immunity of waterfowl to HP IAVs (Pasick et al., 2007; Fereidouni et al., 2009; Berhane et al., 2010, 2014; Costa et al., 2011). Thus, it is plausible that natural infections in wild birds may confer some level of protection to HP IAVs. Similar to studies using previously-exposed waterfowl that were subsequently inoculated with homologous or heterologous LP IAVs, challenge studies assessing HP IAV infections also provide evidence that partial protective immunity conferred from prior homosubtypic or heterosubtypic LP IAV infection may influence infection duration with HP IAVs and associated viral shedding patterns (Fereidouni et al., 2009; Berhane et al., 2010, 2014; Costa et al., 2011). Additionally, prior exposure to LP IAVs may affect outcomes of HP infection in waterfowl. Specifically, partial protective immunity may promote the survival of birds infected with HP IAVs, at least for birds infected with HP viruses that cause disease in immunologically naïve waterfowl (Pasick et al., 2007; Fereidouni et al., 2009; Berhane et al., 2010, 2014; Costa et al., 2011). This suggests that natural LP IAV infections in wild waterfowl followed by infection with HP IAVs could facilitate viral dispersal. Alternatively, prior infection of wild waterfowl to LP IAVs may reduce the duration or magnitude of viral shedding, or provide complete immunity to HP IAVs altogether, therefore reducing the risk of transmission among wild birds in the natural environment (Fereidouni et al., 2009; Berhane et al., 2010, 2014).

2. Summary and conclusions

Through more than a decade of research and surveillance directed towards HP IAVs in wild birds inhabiting North America, we've collectively learned numerous important lessons regarding the feasibility of viruses to be introduced into North America from adjacent regions, the ability of HP IAV infections to be introduced into wild birds and to cross the wild bird-poultry interface, the probability of encounter and detection that may be associated with specific IAV lineages, and how population immunity of wild birds may influence HP IAV outbreak dynamics. These lessons serve as a basis for improving future surveillance activities in North America and help to inform biosecurity practices throughout North America through better understanding of risks associated with IAVs circulating among wild birds in North America and adjacent regions. While future surveillance for HP IAVs in wild birds will undoubtedly lead to additional gains in our understanding of IAV ecology in the natural reservoir and in regards to potential viral threats to domestic poultry, we propose that an increased emphasis on research to better understand mechanisms driving IAV ecology may lead to rapid and meaningful advancements that minimize economic losses associated with HP IAVs in North America. Below we highlight five areas in which we think future mechanistic research relative to IAVs in wild birds in North America are likely to lead to other important lessons learned in the years ahead:

2.1. Role of North American wetlands in the maintenance of IAVs in wild bird populations

Persistence of viruses in aquatic habitats is undoubtedly an important component to IAV ecology (Stallknecht et al., 2010). However, despite extensive sampling of environmental sources in Canada and the USA (Hinshaw et al., 1979; Sivanandan et al., 1991; Ito et al., 1995; Lang et al., 2008; Lebarbenchon et al., 2011) and numerous laboratory investigations to understand how biotic and abiotic factors influence viral persistence (Stallknecht et al., 1990; Brown et al., 2007, 2009; Keeler et al., 2013) it is still unclear how the maintenance of infectious IAVs in North American wetlands influences transmission dynamics or how the persistence of Gs/GD HP IAVs in the environment may have facilitated viral spread during the 2014–2015 outbreak in North America. Furthermore, it is unclear if IAVs can remain infectious in North American wetlands for extended periods, seeding outbreaks in wild birds across seasons or in free-ranging poultry after migratory birds have departed from wintering areas. Future research to understand the persistence of infectious IAVs in the environment at ecologically relevant doses would improve our collective understanding of the role of environmental sources in IAV ecology and improve epidemiological models of transmission (Rohani et al., 2009).

2.2. Transmission of IAVs across the wild bird-poultry interface in North America

Previous studies provide evidence that IAVs circulating among wild birds in North America may lead to introductions of IAVs in poultry production systems for game birds (Ramey et al., 2016e), minor gallinaceous poultry (Bertran et al., 2017), and commercially-reared

chickens and turkeys (Pasick et al., 2012; Guo et al., 2015; Lebarbenchon et al., 2015; Xu et al., 2017). However, few studies have elucidated the mechanisms by which IAVs are able to circumvent biosecurity and infect domestic birds. While numerous investigations have assessed the feasibility of peridomestic birds (Nemeth et al., 2010; Jones et al., 2015; Hall et al., 2016) or mammals (Hall et al., 2008; Root et al., 2014, 2015, 2016, 2017) to serve as bridge species through experimental challenge studies or via surveys assessing prior exposure of free-ranging animals to IAVs, there has been comparatively less effort focused on assessing contact, exposure, and viral transmission between wild and domestic species on poultry farms (Madsen et al., 2013; Shriner et al., 2016; Grear et al., 2017b) or through model systems simulating a wild-domestic animal interface (Achenbach and Bowen, 2011). Furthermore, potential IAV transmission pathways among poultry farms that include spread via worker practices or abiotic mechanisms such as fomites, soil disruption, and viral transport via wind (Garber et al., 2016; Wells et al., 2017) have also been a foci of recent research efforts, but additional data from the field and derived through the development of model systems could improve inference regarding the relative risk of such mechanisms to biosecurity. Although studies assessing transmission of IAVs across the wild bird-poultry interface may be complex in nature and challenging to implement, ultimately, research efforts in this field are likely to result in meaningful inference with regards to identifying ways in which biosecurity may be improved to protect North American poultry holdings.

2.3. Genetic determinants conferring adaptations of IAVs to both waterfowl and poultry

Genetic determinants conferring adaptation of wild bird origin IAVs to gallinaceous poultry and affecting virulence in chickens is well described for the HA gene (Senne et al., 1996). However, more recent evidence suggests that genetic determinants for IAV replication and virulence in domestic poultry are multigenic (Hossain et al., 2008; Wasilenko et al., 2008; Sorrell et al., 2010; Munier et al., 2010). Less well-defined are specific adaptations that facilitate efficient replication of IAVs in both waterfowl and domestic gallinaceous birds. Such IAVs, containing genetic determinants suggestive of efficient replication in both wild and domestic avian hosts, may be useful for identifying potential biosecurity threats through surveillance efforts and for informing vaccine development. While limitations on gain of function studies may impede progress in this research area, comparative genetic approaches utilizing data from wild bird and domestic poultry surveillance may facilitate continued progress towards understanding the adaptation of IAVs to multiple avian hosts.

2.4. Infectivity of H5 Gs/GD lineage HP IAVs in North American waterfowl species

Although it is unclear if H5 Gs/GD lineage HP IAVs remain in North America, such viruses have circulated in East Asia for more than 20 years and continue to cause periodic outbreaks among wild and domestic birds throughout this region and elsewhere (Fusaro et al., 2017; Kwon et al., 2017; Lee et al., 2017b; Li et al., 2017; Okamatsu et al., 2017; Pohlmann et al., 2017; Selim et al., 2017). Thus, it is plausible that these viruses may be again introduced into wild birds in Canada and the USA. As such, additional information regarding the infectivity, adaptation, and pathogenicity of Gs/GD lineage HP H5 IAVs in North American wild birds would be useful for better understanding the potential for dispersal via migratory movements and possible impacts to avian populations in Canada and the USA. It should be noted that, while Gs/GD lineage HP H5 IAVs may share common ancestry with regard to the HA gene, experimental challenge studies suggest differences in infectivity, adaptation, and pathogenicity among strains of this viral lineage in North American birds (Pantin-Jackwood et al., 2016). Furthermore, North American wild bird species appear to vary in their susceptibility to infection and disease when infected with the same Gs/GD viral strain (Brown et al., 2006). As such, future studies should be designed and adapted in such a manner to provide relevant information for North American wild bird species in response to continued viral evolution and perceived risk of introduction to specific populations (e.g., particular species or avian communities inhabiting geographic areas of interest).

2.5. Immune response of wild birds to emergent HP IAVs detected in poultry

Information on how the 2014–2015 outbreak of H5 Gs/GD lineage clade 2.3.4.4 HP IAV in North America affected population immunity of wild waterfowl and other free-ranging avian taxa in Canada and the USA is currently lacking. Furthermore, it is unknown how population immunity may have affected outbreak dynamics. Given the evidence for the role of population immunity as a driver of IAV ecology in wild waterfowl (Latorre-Margalef et al., 2013) and the potential for future introductions of HP IAVs into wild birds inhabiting North America, particularly from East Asia, research efforts to understand the immune response of wild birds to emergent HP IAVs detected in poultry could prove useful towards evaluating the relative risk of viral dispersal via wild birds, assessing the likelihood of HP IAV establishment among free-ranging avian taxa, and forecasting outbreak dynamics. Research conducted in this area may be a natural extension of efforts to better understand infectivity of HP IAVs in North American waterfowl species.

Acknowledgements

We thank all scientists in North America and elsewhere that have conducted research and surveillance directed at highly pathogenic influenza A viruses in wild birds over the past 50 years for all their contributions towards the advancement of our collective understanding of this topic. We appreciate constructive reviews on prior drafts of this manuscript provided by John Pearce, Diann Prosser, and two anonymous reviewers. This summary was funded, in part, by the U.S. Geological Survey through the Wildlife Program of the Ecosystems Mission area. Any use of trade names is for descriptive purposes only and does not imply endorsement by the U.S. Government.

References

Achenbach, J.E., Bowen, R.A., 2011. Transmission of avian influenza A viruses among species in an artificial barnyard. PLoS One 6 (3) (p.e17643).
Berhane, Y., Hisanaga, T., Kehler, H., Neufeld, J., Manning, L., Argue, C., Handel, K., Hooper-McGrevy, K., Jonas, M., Robinson, J., Webster, R.G., 2009. Highly pathogenic avian influenza virus A (H7N3) in domestic poultry, Saskatchewan, Canada, 2007. Emerg. Infect. Dis. 15 (9) (p.1492).
Berhane, Y., Leith, M., Embury-Hyatt, C., Neufeld, J., Babiuk, S., Hisanaga, T., Kehler, H., Hooper-McGrevy, K., Pasick, J., 2010. Studying possible cross-protection of Canada geese preexposed to North American low pathogenicity avian influenza virus strains (H3N8, H4N6, and H5N2) against an H5N1 highly pathogenic avian influenza challenge. Avian Dis. 54 (s1), 548–554.
Berhane, Y., Embury-Hyatt, C., Leith, M., Kehler, H., Suderman, M., Pasick, J., 2014. Pre-exposing Canada Geese (Branta canadensis) to a low-pathogenic H1N1 avian influenza virus protects them against H5N1 HPAI virus challenge. J. Wildl. Dis. 50 (1), 84–97.
Berhane, Y., Kobasa, D., Embury-Hyatt, C., Pickering, B., Babiuk, S., Joseph, T., Bowes, V., Suderman, M., Leung, A., Cottam-Birt, C., Hisanaga, T., 2016. Pathobiological characterization of a novel reassortant highly pathogenic H5N1 virus isolated in British Columbia, Canada, 2015. Sci. Rep. 6 (p.23380).
Bertran, K., Lee, D.H., Pantin-Jackwood, M.J., Spackman, E., Balzli, C., Suarez, D.L., Swayne, D.E., 2017. Pathobiology of clade 2.3. 4.4 H5Nx high pathogenicity avian influenza virus infections in minor gallinaceous poultry supports early backyard flock introductions in Western US, 2014–2015. J. Virol (pp.JVI-00960).
Bevins, S.N., Dusek, R.J., White, C.L., Gidlewski, T., Bodenstein, B., Mansfield, K.G., DeBruyn, P., Kraege, D., Rowan, E., Gillin, C., Thomas, B., 2016. Widespread detection of highly pathogenic H5 influenza viruses in wild birds from the Pacific Flyway of the United States. Sci. Rep. 6.
Boyce, W.M., Schobel, S., Dugan, V.G., Halpin, R., Lin, X., Wentworth, D.E., Lindsay, L.L., Mertens, E., Plancarte, M., 2013. Complete genome sequence of a reassortant H14N2 avian influenza virus from California. Genome Announc. 1 (4), e00543–13.
Brown, J.D., Stallknecht, D.E., Beck, J.R., Suarez, D.L., Swayne, D.E., 2006. Susceptibility of North American ducks and gulls to H5N1 highly pathogenic avian influenza

viruses. Emerg. Infect. Dis. 12 (11) (p.1663).
Brown, J.D., Swayne, D.E., Cooper, R.J., Burns, R.E., Stallknecht, D.E., 2007. Persistence of H5 and H7 avian influenza viruses in water. Avian Dis. 51 (Suppl. 1), 285–289.
Brown, J.D., Goekjian, G., Poulson, R., Valeika, S., Stallknecht, D.E., 2009. Avian influenza virus in water: infectivity is dependent on pH, salinity and temperature. Vet. Microbiol. 136 (1), 20–26.
Buisch, W.W., Hall, A.E., McDaniel, H.A., 1984. 1983–1984 lethal avian influenza outbreak. In: Proceedings 88th Annual Meeting of the United States Animal Health Association (USA), vol. 88, pp. 430–446.
Chen, H., Smith, G.J.D., Zhang, S.Y., Qin, K., 2005. H5N1 virus outbreak in migratory waterfowl. Nature 436 (7048) (p.191).
Costa, T.P., Brown, J.D., Howerth, E.W., Stallknecht, D.E., 2010. Effect of a prior exposure to a low pathogenic avian influenza virus in the outcome of a heterosubtypic low pathogenic avian influenza infection in mallards (*Anas platyrhynchos*). Avian Dis. 1286–1291.
Costa, T.P., Brown, J.D., Howerth, E.W., Stallknecht, D.E., Swayne, D.E., 2011. Homo-and heterosubtypic low pathogenic avian influenza exposure on H5N1 highly pathogenic avian influenza virus infection in wood ducks (*Aix sponsa*). PLoS One 6 (1) (p.e15987).
DeJesus, E., Costa-Hurtado, M., Smith, D., Lee, D.H., Spackman, E., Kapczynski, D.R., Torchetti, M.K., Killian, M.L., Suarez, D.L., Swayne, D.E., Pantin-Jackwood, M.J., 2016. Changes in adaptation of H5N2 highly pathogenic avian influenza H5 clade 2.3. 4.4 viruses in chickens and mallards. Virology 499, 52–64.
Douglas, K.O., Lavoie, M.C., Mia Kim, L., Afonso, C.L., Suarez, D.L., 2007. Isolation and genetic characterization of avian influenza viruses and a Newcastle disease virus from wild birds in Barbados: 2003–2004. Avian Dis. 51 (3), 781–787.
Easterday, B.C., Trainer, D.O., Tůmová, B., Pereira, H.G., 1968. Evidence of infection with influenza viruses in migratory waterfowl. Nature 219 (5153), 523–524.
Ellis, T.M., Barry Bousfield, R., Bissett, L.A., Dyrting, K.C., Luk, G.S., Tsim, S.T., Sturm-Ramirez, K., Webster, R.G., Guan, Y., Peiris, J.M., 2004. Investigation of outbreaks of highly pathogenic H5N1 avian influenza in waterfowl and wild birds in Hong Kong in late 2002. Avian Pathol. 33 (5), 492–505.
Fereidouni, S.R., Starick, E., Beer, M., Wilking, H., Kalthoff, D., Grund, C., Häuslaigner, R., Breithaupt, A., Lange, E., Harder, T.C., 2009. Highly pathogenic avian influenza virus infection of mallards with homo-and heterosubtypic immunity induced by low pathogenic avian influenza viruses. PLoS One 4 (8) (p.e6706).
Fries, A.C., Nolting, J.M., Danner, A., Webster, R.G., Bowman, A.S., Krauss, S., Slemons, R.D., 2013. Evidence for the circulation and inter-hemispheric movement of the H14 subtype influenza A virus. PLoS One 8 (3) (p.e59216).
Fries, A.C., Nolting, J.M., Bowman, A.S., Killian, M.L., Wentworth, D.E., Slemons, R.D., 2014. Genomic analyses detect Eurasian-lineage H10 and additional H14 influenza A viruses recovered from waterfowl in the Central United States. Influenza Other Respir. Virus. 8 (4), 493–498.
Fusaro, A., Monne, I., Mulatti, P., Zecchin, B., Bonfanti, L., Ormelli, S., Milani, A., Cecchettin, K., Lemey, P., Moreno, A., Massi, P., 2017. Genetic diversity of highly pathogenic avian influenza A (H5N8/H5N5) viruses in Italy, 2016–17. Emerg. Infect. Dis. 23 (9) (p.1543).
Garber, L., Bjork, K., Patyk, K., Rawdon, T., Antognoli, M., Delgado, A., Ahola, S., McCluskey, B., 2016. Factors associated with highly pathogenic avian influenza H5N2 infection on table-egg layer farms in the midwestern United States, 2015. Avian Dis. 60 (2), 460–466.
González-Reiche, A.S., Morales-Betoulle, M.E., Alvarez, D., Betoulle, J.L., Müller, M.L., Sosa, S.M., Perez, D.R., 2012. Influenza A viruses from wild birds in Guatemala belong to the North American lineage. PLoS One 7 (3) (p.e32873).
Gonzalez-Reiche, A.S., Müller, M.L., Ortiz, L., Cordón-Rosales, C., Perez, D.R., 2016. Prevalence and diversity of low pathogenicity avian influenza viruses in wild birds in Guatemala, 2010–2013. Avian Dis. 60 (Suppl. 1), 359–364.
Grear, D., Hall, J.S., Dusek, R., Ip, H.S., 2018a. Inferring epidemiologic dynamics from viral evolution: 2014–2015 Eurasian/North American highly pathogenic avian influenza viruses exceed transmission threshold, R0 = 1, in wild birds and poultry in North America. Evolut. Appl (in press).
Grear, D.A., Dusek, R.J., Walsh, D.P., Hall, J.S., 2017b. No evidence of infection or exposure to Highly Pathogenic Avian Influenzas in peridomestic wildlife on an affected poultry facility. J. Wildl. Dis. 53 (1), 37–45.
Guo, X., Flores, C., Munoz-Aguayo, J., Halvorson, D.A., Lauer, D., Cardona, C.J., 2015. Historical and recent cases of H3 Influenza A virus in turkeys in minnesota. Avian Dis. 59 (4), 512–517.
Hall, J.S., Bentler, K.T., Landolt, G., Elmore, S.A., Minnis, R.B., Campbell, T.A., Barras, S.C., Root, J.J., Pilon, J., Pabilonia, K., Driscoll, C., 2008. Influenza infection in wild raccoons. Emerg. Infect. Dis. 14 (12) (p.1842).
Hall, J.S., Ip, H.S., TeSlaa, J.L., Nashold, S.W., Dusek, R.J., 2016. Experimental challenge of a peridomestic avian species, European starlings (*Sturnus vulgaris*), with novel influenza A H7N9 virus from China. J. Wildl. Dis. 52 (3), 709–712.
Hill, N.J., Hussein, I.T., Davis, K.R., Ma, E.J., Spivey, T.J., Ramey, A.M., Puryear, W.B., Das, S.R., Halpin, R.A., Lin, X., Fedorova, N.B., 2017. Reassortment of influenza A viruses in wild birds in Alaska before H5 Clade 2.3. 4.4 outbreaks. Emerg. Infect. Dis. 23 (4) (p.654).
Hinshaw, V.S., Webster, R.G., Turner, B., 1979. Water-borne transmission of influenza A viruses? Intervirology 11 (1), 66–68.
Hinshaw, V.S., Webster, R.G., Turner, B., 1980. The perpetuation of orthomyxoviruses and paramyxoviruses in Canadian waterfowl. Can. J. Microbiol. 26 (5), 622–629.
Hirst, M., Astell, C.R., Griffith, M., Coughlin, S.M., Moksa, M., Zeng, T., Smailus, D.E., Holt, R.A., Jones, S., Marra, M.A., Petric, M., 2004. Novel avian influenza H7N3 strain outbreak, British Columbia. Emerg. Infect. Dis. 10 (12) (p.2192).
Hossain, M.J., Hickman, D., Perez, D.R., 2008. Evidence of expanded host range and mammalian-associated genetic changes in a duck H9N2 influenza virus following adaptation in quail and chickens. PLoS One 3 (9) (p.e3170).
Hu, T., Song, J., Zhang, W., Zhao, H., Duan, B., Liu, Q., Zeng, W., Qiu, W., Chen, G., Zhang, Y., Fan, Q., 2015. Emergence of novel clade 2.3. 4 influenza A (H5N1) virus subgroups in Yunnan Province, China. Infect. Genet. Evol. 33, 95–100.
Huang, Y., Robertson, G.J., Ojkic, D., Whitney, H., Lang, A.S., 2014a. Diverse intercontinental and host lineage reassortant avian influenza A viruses in pelagic seabirds. Infect. Genet. Evol. 22, 103–111.
Huang, Y., Wille, M., Benkaroun, J., Munro, H., Bond, A.L., Fifield, D.A., Robertson, G.J., Ojkic, D., Whitney, H., Lang, A.S., 2014b. Perpetuation and reassortment of gull influenza A viruses in Atlantic North America. Virology 456, 353–363.
Hulse-Post, D.J., Sturm-Ramirez, K.M., Humberd, J., Seiler, P., Govorkova, E.A., Krauss, S., Scholtissek, C., Puthavathana, P., Buranathai, C., Nguyen, T.D., Long, H.T., 2005. Role of domestic ducks in the propagation and biological evolution of highly pathogenic H5N1 influenza viruses in Asia. Proc. Natl. Acad. Sci. USA 102 (30), 10682–10687.
Hupp, J.W., Schmutz, J.A., Ely, C.R., Syroechkovskiy, E.E., Kondratyev, A.V., Eldridge, W.D., Lappo, E., 2007. Moult migration of emperor geese *Chen canagica* between Alaska and Russia. J. Avian Biol. 38, 462–470.
Hupp, J.W., Yamaguchi, N., Flint, P.L., Pearce, J.M., Tokita, K., Shimada, T., Ramey, A.M., Kharitonov, S., Higuchi, H., 2011. Variation in spring migration routes and breeding distribution of northern pintails *Anas acuta* that winter in Japan. J. Avian Biol. 42, 289–300.
Ip, H.S., Torchetti, M.K., Crespo, R., Kohrs, P., DeBruyn, P., Mansfield, K.G., Baszler, T., Badcoe, L., Bodenstein, B., Shearn-Bochsler, V., Killian, M.L., 2015. Novel Eurasian highly pathogenic avian influenza A H5 viruses in wild birds, Washington, USA, 2014. Emerg. Infect. Dis. 21 (5) (p.886).
Ito, T., Okazaki, K., Kawaoka, Y., Takada, A., Webster, R.G., Kida, H., 1995. Perpetuation of influenza A viruses in Alaskan waterfowl reservoirs. Arch. Virol. 140 (7), 1163–1172.
Jhung, M.A., Nelson, D.I., Centers for Disease Control and Prevention (CDC), 2015. Outbreaks of avian influenza A (H5N2),(H5N8), and (H5N1) among birds—United States, December 2014–January 2015. Morb. Mortal. Wkly. Rep. 64 (4) (p.111).
Jones, J.C., Sonnberg, S., Webby, R.J., Webster, R.G., 2015. Influenza A (H7N9) virus transmission between finches and poultry. Emerg. Infect. Dis. 21 (4) (p.619).
Jourdain, E., Gunnarsson, G., Wahlgren, J., Latorre-Margalef, N., Bröjer, C., Sahlin, S., Svensson, L., Waldenström, J., Lundkvist, Å., Olsen, B., 2010. Influenza virus in a natural host, the mallard: experimental infection data. PLoS One 5 (1) (p.e8935).
Karlsson, E.A., Ciuoderis, K., Freiden, P.J., Seufzer, B., Jones, J.C., Johnson, J., Parra, R., Gongora, A., Cardenas, D., Barajas, D., Osorio, J.E., 2013. Prevalence and characterization of influenza viruses in diverse species in Los Llanos, Colombia. Emerg. Microbes Infect. 2 (4) (p.e20).
Kawaoka, Y., Yamnikova, S., Chambers, T.M., Lvov, D.K., Webster, R.G., 1990. Molecular characterization of a new hemagglutinin, subtype H14, of influenza A virus. Virology 179 (2), 759–767.
Keeler, S.P., Lebarbenchon, C., Stallknecht, D.E., 2013. Strain-related variation in the persistence of influenza A virus in three types of water: distilled water, filtered surface water, and intact surface water. Virol. J. 10 (1) (p.13).
Killian, M.L., Kim-Torchetti, M., Hines, N., Yingst, S., DeLiberto, T., Lee, D.H., 2016. Outbreak of H7N8 low pathogenic avian influenza in commercial turkeys with spontaneous mutation to highly pathogenic avian influenza. Genome Announc. 4 (3) (pp.e00457-16).
Koehler, A.V., Pearce, J.M., Flint, P.L., Franson, J.C., Ip, H.S., 2008. Genetic evidence of intercontinental movement of avian influenza in a migratory bird: the northern pintail (*Anas acuta*). Mol. Ecol. 17 (21), 4754–4762.
Krauss, S., Obert, C.A., Franks, J., Walker, D., Jones, K., Seiler, P., Niles, L., Pryor, S.P., Obenauer, J.C., Naeve, C.W., Widjaja, L., 2007. Influenza in migratory birds and evidence of limited intercontinental virus exchange. PLoS Pathog. 3 (11) (p.e167).
Krauss, S., Stallknecht, D.E., Slemons, R.D., Bowman, A.S., Poulson, R.L., Nolting, J.M., Knowles, J.P., Webster, R.G., 2016. The enigma of the apparent disappearance of Eurasian highly pathogenic H5 clade 2.3. 4.4 influenza A viruses in North American waterfowl. Proc. Natl. Acad. Sci. USA 113 (32), 9033–9038.
Kwon, J.H., Lee, D.H., Swayne, D.E., Noh, J.Y., Yuk, S.S., Erdene-Ochir, T.O., Hong, W.T., Jeong, J.H., Jeong, S., Gwon, G.B., Lee, S., 2017. Reassortant clade 2.3. 4.4 avian influenza A (H5N6) virus in a wild mandarin duck, South Korea, 2016. Emerg. Infect. Dis. 23 (5) (p.822).
Lang, A.S., Kelly, A., Runstadler, J.A., 2008. Prevalence and diversity of avian influenza viruses in environmental reservoirs. J. Gen. Virol. 89 (2), 509–519.
Latorre-Margalef, N., Grosbois, V., Wahlgren, J., Munster, V.J., Tolf, C., Fouchier, R.A., Osterhaus, A.D., Olsen, B., Waldenström, J., 2013. Heterosubtypic immunity to influenza A virus infections in mallards may explain existence of multiple virus subtypes. PLoS Pathog. 9 (6) (p.e1003443).
Latorre-Margalef, N., Brown, J.D., Fojtik, A., Poulson, R.L., Carter, D., Franca, M., Stallknecht, D.E., 2017. Competition between influenza A virus subtypes through heterosubtypic immunity modulates re-infection and antibody dynamics in the mallard duck. PLoS Pathog. 13 (6) (p.e1006419).
Lebarbenchon, C., Keeler, S.P., Ramakrishnan, M.A., Brown, J.D., Stallknecht, D.E., Sreevatsan, S., 2011. Viral replication, persistence in water and genetic characterization of two influenza A viruses isolated from surface lake water. PLoS One 6 (10) (p.e26566).
Lebarbenchon, C., Pedersen, J.C., Sreevatsan, S., Ramey, A.M., Dugan, V.G., Halpin, R.A., Ferro, P.J., Lupiani, B., Enomoto, S., Poulson, R.L., Smeltzer, M., 2015. H7N9 influenza A virus in turkeys in Minnesota. J. Gen. Virol. 96 (2), 269–276.
Lee, C.W., Swayne, D.E., Linares, J.A., Senne, D.A., Suarez, D.L., 2005. H5N2 avian influenza outbreak in Texas in 2004: the first highly pathogenic strain in the United States in 20 years? J. Virol. 79 (17), 11412–11421.
Lee, D.H., Torchetti, M.K., Winker, K., Ip, H.S., Song, C.S., Swayne, D.E., 2015.

Intercontinental spread of Asian-origin H5N8 to North America through Beringia by migratory birds. J. Virol. 89 (12), 6521–6524.
Lee, D.H., Kwon, J.H., Park, J.K., Yuk, S.S., Tseren-Ochir, E.O., Noh, J.Y., Lee, J.B., Park, S.Y., Choi, I.S., Song, C.S., 2016a. Experimental infection of chickens with intercontinental reassortant H9N2 influenza viruses from Wild Birds. Avian Dis. 60 (2), 493–495.
Lee, D.H., Bahl, J., Torchetti, M.K., Killian, M.L., Ip, H.S., DeLiberto, T.J., Swayne, D.E., 2016b. Highly pathogenic avian influenza viruses and generation of novel reassortants, United States, 2014–2015. Emerg. Infect. Dis. 22 (7) (p.1283).
Lee, D.H., Torchetti, M.K., Killian, M.L., DeLiberto, T.J., Swayne, D.E., 2017a. Reoccurrence of avian influenza A (H5N2) virus clade 2.3.4.4 in wild birds, Alaska, USA, 2016. Emerg. Infect. Dis. 23 (2) (p.365).
Lee, D.H., Sharshov, K., Swayne, D.E., Kurskaya, O., Sobolev, I., Kabilov, M., Alekseev, A., Irza, V., Shestopalov, A., 2017b. Novel reassortant clade 2.3. 4.4 avian influenza A (H5N8) virus in wild aquatic birds, Russia, 2016. Emerg. Infect. Dis. 23 (2) (p.359).
Lee, D.H., Bertran, K., Kwon, J.H., Swayne, D.E., 2017c. Evolution, global spread, and pathogenicity of highly pathogenic avian influenza H5Nx clade 2.3.4.4. J. Vet. Sci. 18 (S1), 269–280.
Li, M., Liu, H., Bi, Y., Sun, J., Wong, G., Liu, D., Li, L., Liu, J., Chen, Q., Wang, H., He, Y., 2017. Highly pathogenic avian Influenza A (H5N8) virus in wild migratory birds, Qinghai Lake, China. Emerg. Infect. Dis. 23 (4), 637.
Lycett, S.J., Bodewes, R., Pohlmann, A., Banks, J., Bányai, K., et al., 2016. Role for migratory wild birds in the global spread of avian influenza H5N8. Science 354 (6309), 213–217.
Madsen, J.M., Zimmermann, N.G., Timmons, J., Tablante, N.L., 2013. Avian influenza seroprevalence and biosecurity risk factors in Maryland backyard poultry: a cross-sectional study. PLoS One 8 (2) (p.e56851).
Miller, M.R., Takekawa, J.Y., Fleskes, J.P., Orthmeyer, D.L., Casazza, M.L., Perry, W.M., 2005. Spring migration of Northern Pintails from California's Central Valley wintering area tracked with satellite telemetry: routes, timing, and destinations. Can. J. Zool. 83 (10), 1314–1332.
Munier, S., Larcher, T., Cormier-Aline, F., Soubieux, D., Su, B., Guigand, L., Labrosse, B., Cherel, Y., Quéré, P., Marc, D., Naffakh, N., 2010. A genetically engineered waterfowl influenza virus with a deletion in the stalk of the neuraminidase has increased virulence for chickens. J. Virol. 84 (2), 940–952.
Nemeth, N.M., Thomas, N.O., Orahood, D.S., Anderson, T.D., Oesterle, P.T., 2010. Shedding and serologic responses following primary and secondary inoculation of house sparrows (*Passer domesticus*) and European starlings (*Sturnus vulgaris*) with low-pathogenicity avian influenza virus. Avian Pathol. 39 (5), 411–418.
Nolting, J., Fries, A.C., Slemons, R.D., Courtney, C., Hines, N., Pedersen, J., 2012. Recovery of H14 influenza A virus isolates from sea ducks in the Western Hemisphere. PLoS Curr. 4.
Office International des Epizooties, Immediate notification report. 2015. 'Report Reference: CAN-2015-NAI-003 REF OIE 17577' available at: 〈http://www.oie.int/wahis_2/public%5C.%5Ctemp%5Creports/en_imm_0000017577_20150504_174330.pdf〉 (Last accessed 6 September 2017).
Okamatsu, M., Ozawa, M., Soda, K., Takakuwa, H., Haga, A., Hiono, T., Matsuu, A., Uchida, Y., Iwata, R., Matsuno, K., Kuwahara, M., 2017. Characterization of highly pathogenic avian Influenza Virus A (H5N6), Japan, November 2016. Emerg. Infect. Dis. 23 (4) (p.691).
Pantin-Jackwood, M.J., Costa-Hurtado, M., Shepherd, E., DeJesus, E., Smith, D., Spackman, E., Kapczynski, D.R., Suarez, D.L., Stallknecht, D.E., Swayne, D.E., 2016. Pathogenicity and transmission of H5 and H7 highly pathogenic avian influenza viruses in mallards. J. Virol. 90 (21), 9967–9982.
Pasick, J., Handel, K., Robinson, J., Copps, J., Ridd, D., Hills, K., Kehler, H., Cottam-Birt, C., Neufeld, J., Berhane, Y., Czub, S., 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 (3), 727–731.
Pasick, J., Berhane, Y., Embury-Hyatt, C., Copps, J., Kehler, H., Handel, K., Babiuk, S., Hooper-McGrevy, K., Li, Y., Le, Q.M., Phuong, S.L., 2007. Susceptibility of Canada geese (*Branta canadensis*) to highly pathogenic avian influenza virus (H5N1). Emerg. Infect. Dis. 13 (12) (p.1821).
Pasick, J., Pedersen, J., Hernandez, M.S., 2012. Avian influenza in North America, 2009–2011. Avian Dis. 56 (4s1), 845–848.
Pasick, J., Berhane, Y., Joseph, T., Bowes, V., Hisanaga, T., Handel, K., Alexandersen, S., 2015. Reassortant highly pathogenic influenza A H5N2 virus containing gene segments related to Eurasian H5N8 in British Columbia, Canada, 2014. Sci. Rep. 5.
Pearce, J.M., Ramey, A.M., Flint, P.L., Koehler, A.V., Fleskes, J.P., Franson, J.C., Hall, J.S., Derksen, D.V., Ip, H.S., 2009. Avian influenza at both ends of a migratory flyway: characterizing viral genomic diversity to optimize surveillance plans for North America. Evolut. Appl. 2 (4), 457–468.
Pelzel, A.M., McCluskey, B.J., Scott, A.E., 2006. Review of the highly pathogenic avian influenza outbreak in Texas, 2004. J. Am. Vet. Med. Assoc. 228 (12), 1869–1875.
Pepin, K.M., VanDalen, K.K., Mooers, N.L., Ellis, J.W., Sullivan, H.J., Root, J.J., Webb, C.T., Franklin, A.B., Shriner, S.A., 2012. Quantification of heterosubtypic immunity between avian influenza subtypes H3N8 and H4N6 in multiple avian host species. J. Gen. Virol. 93 (12), 2575–2583.
Perkins, L.E.L., Swayne, D.E., 2003. Comparative susceptibility of selected avian and mammalian species to a Hong Kong-origin H5N1 highly pathogenic avian influenza virus. Avian Dis. 47, 956–967.
Ping, J., Selman, M., Tyler, S., Forbes, N., Keleta, L., Brown, E.G., 2012. Low-pathogenic avian influenza virus A/turkey/Ontario/6213/1966 (H5N1) is the progenitor of highly pathogenic A/turkey/Ontario/7732/1966 (H5N9). J. Gen. Virol. 93 (8), 1649–1657.
Pohlmann, A., Starick, E., Harder, T., Grund, C., Höper, D., Globig, A., Staubach, C., Dietze, K., Strebelow, G., Ulrich, R.G., Schinköthe, J., 2017. Outbreaks among wild birds and domestic poultry caused by reassorted influenza A (H5N8) clade 2.3. 4.4 viruses, Germany, 2016. Emerg. Infect. Dis. 23 (4) (p.633).
Ramey, A.M., Pearce, J.M., Flint, P.L., Ip, H.S., Derksen, D.V., Franson, J.C., Petrula, M.J., Scotton, B.D., Sowl, K.M., Wege, M.L., Trust, K.A., 2010a. Intercontinental reassortment and genomic variation of low pathogenic avian influenza viruses isolated from northern pintails (*Anas acuta*) in Alaska: examining the evidence through space and time. Virology 401 (2), 179–189.
Ramey, A.M., Pearce, J.M., Ely, C.R., Guy, L.M.S., Irons, D.B., Derksen, D.V., Ip, H.S., 2010b. Transmission and reassortment of avian influenza viruses at the Asian–North American interface. Virology 406 (2), 352–359.
Ramey, A.M., Pearce, J.M., Reeves, A.B., Franson, J.C., Petersen, M.R., Ip, H.S., 2011. Evidence for limited exchange of avian influenza viruses between seaducks and dabbling ducks at Alaska Peninsula coastal lagoons. Arch. Virol. 156 (10) (1813).
Ramey, A.M., Poulson, R.L., González-Reiche, A.S., Wilcox, B.R., Walther, P., Link, P., Carter, D.L., Newsome, G.M., Müller, M.L., Berghaus, R.D., Perez, D.R., 2014a. Evidence for seasonal patterns in the relative abundance of avian influenza virus subtypes in blue-winged teal (*Anas discors*). J. Wildl. Dis. 50 (4), 916–922.
Ramey, A.M., Poulson, R.L., González-Reiche, A.S., Perez, D.R., Stallknecht, D.E., Brown, J.D., 2014b. Genomic characterization of H14 subtype influenza A viruses in new world waterfowl and experimental infectivity in mallards (*Anas platyrhynchos*). PLoS One 9 (5) (p.e95620).
Ramey, A.M., Reeves, A.B., Sonsthagen, S.A., TeSlaa, J.L., Nashold, S., Donnelly, T., Casler, B., Hall, J.S., 2015. Dispersal of H9N2 influenza A viruses between East Asia and North America by wild birds. Virology 482, 79–83.
Ramey, A.M., Reeves, A.B., TeSlaa, J.L., Nashold, S., Donnelly, T., Bahl, J., Hall, J.S., 2016a. Evidence for common ancestry among viruses isolated from wild birds in Beringia and highly pathogenic intercontinental reassortant H5N1 and H5N2 influenza A viruses. Infect. Genet. Evol. 40, 176–185.
Ramey, A.M., Walther, P., Link, P., Poulson, R.L., Wilcox, B.R., Newsome, G., Spackman, E., Brown, J.D., Stallknecht, D.E., 2016b. Optimizing surveillance for South American origin influenza A viruses along the United States Gulf Coast through genomic characterization of isolates from blue-winged teal (*Anas discors*). Transbound. Emerg. Dis. 63 (2), 194–202.
Ramey, A.M., Reeves, A.B., Poulson, R.L., Carter, D.L., Davis-Fields, N., Stallknecht, D.E., 2016c. Genome sequence of a novel H14N7 subtype influenza A virus isolated from a blue-winged teal (*Anas discors*) harvested in Texas, USA. Genome Announc. 4 (3), e00520–16.
Ramey, A.M., Pearce, J.M., Reeves, A.B., Poulson, R.L., Dobson, J., Lefferts, B., Spragens, K., Stallknecht, D.E., 2016d. Surveillance for Eurasian-origin and intercontinental reassortant highly pathogenic influenza A viruses in Alaska, spring and summer 2015. Virol. J. 13 (1) (p.55).
Ramey, A.M., Torchetti, M.K., Poulson, R.L., Carter, D., Reeves, A.B., Link, P., Walther, P., Lebarbenchon, C., Stallknecht, D.E., 2016e. Evidence for wild waterfowl origin of H7N3 influenza A virus detected in captive-reared New Jersey pheasants. Arch. Virol. 161 (9), 2519–2526.
Ramey, A.M., Hill, N.J., Cline, T., Plancarte, M., De La Cruz, S., Casazza, M.L., Ackerman, J.T., Fleskes, J.P., Vickers, T.W., Reeves, A.B., Gulland, F., Fontaine, C., Prosser, D.J., Runstadler, J.A., Boyce, W.M., 2017. Surveillance for highly pathogenic influenza A viruses in California during 2014–2015 provides insights into evolutionary pathways and spatiotemporal extent in the Pacific Americas Flyway. Emerg. Microbes Infect. 6 (e80).
Reeves, A.B., Pearce, J.M., Ramey, A.M., Ely, C.R., Schmutz, J.A., Flint, P.L., Derksen, D.V., Ip, H.S., Trust, K.A., 2013. Genomic analysis of avian influenza viruses from waterfowl in western Alaska, USA. J. Wildl. Dis. 49 (3), 600–610.
Rohani, P., Breban, R., Stallknecht, D.E., Drake, J.M., 2009. Environmental transmission of low pathogenicity avian influenza viruses and its implications for pathogen invasion. Proc. Natl. Acad. Sci. USA 106 (25), 10365–10369.
Root, J.J., Shriner, S.A., Bentler, K.T., Gidlewski, T., Mooers, N.L., Ellis, J.W., Spraker, T.R., VanDalen, K.K., Sullivan, H.J., Franklin, A.B., 2014. Extended viral shedding of a low pathogenic avian influenza virus by striped skunks (*Mephitis mephitis*). PLoS One 9 (1) (p.e70639).
Root, J.J., Shriner, S.A., Ellis, J.W., VanDalen, K.K., Sullivan, H.J., Franklin, A.B., 2015. When fur and feather occur together: interclass transmission of avian influenza A virus from mammals to birds through common resources. Sci. Rep. 5.
Root, J.J., Bosco-Lauth, A.M., Bielefeldt-Ohmann, H., Bowen, R.A., 2016. Experimental infection of peridomestic mammals with emergent H7N9 (A/Anhui/1/2013) influenza A virus: implications for biosecurity and wet markets. Virology 487, 242–248.
Root, J.J., Shriner, S.A., Ellis, J.W., VanDalen, K.K., Sullivan, H.J., 2017. Low viral doses are sufficient to infect cottontail rabbits with avian influenza A virus. Arch. Virol. 1–8.
Segovia, K.M., Stallknecht, D.E., Kapczynski, D.R., Stabler, L., Berghaus, R.D., Fotjik, A., Latorre-Margalef, N., França, M.S., 2017. Adaptive heterosubtypic immunity to low pathogenic avian influenza viruses in experimentally infected mallards. PLoS One 12 (1), e0170335.
Selim, A.A., Erfan, A.M., Hagag, N., Zanaty, A., Samir, A.H., Samy, M., Abdelhalim, A., Arafa, A.S.A., Soliman, M.A., Shaheen, M., Ibraheem, E.M., 2017. Highly pathogenic avian influenza virus (H5N8) clade 2.3. 4.4 infection in migratory birds, Egypt. Emerg. Infect. Dis. 23 (6), 1048.
Senne, D.A., Panigrahy, B., Kawaoka, Y., Pearson, J.E., Süss, J., Lipkind, M., Kida, H., Webster, R.G., 1996. Survey of the hemagglutinin (HA) cleavage site sequence of H5 and H7 avian influenza viruses: amino acid sequence at the HA cleavage site as a marker of pathogenicity potential. Avian Dis. 425–437.
Shriner, S.A., Root, J.J., Lutman, M.W., Kloft, J.M., VanDalen, K.K., Sullivan, H.J., White, T.S., Milleson, M.P., Hairston, J.L., Chandler, S.C., Wolf, P.C., 2016. Surveillance for highly pathogenic H5 avian influenza virus in synanthropic wildlife associated with

poultry farms during an acute outbreak. Sci. Rep. 6 (p.36237).
Sivanandan, V., Halvorson, D.A., Laudert, E., Senne, D.A., Kumar, M.C., 1991. Isolation of H13N2 influenza A virus from turkeys and surface water. Avian Dis. 974–977.
Sorrell, E.M., Song, H., Pena, L., Perez, D.R., 2010. A 27-amino-acid deletion in the neuraminidase stalk supports replication of an avian H2N2 influenza A virus in the respiratory tract of chickens. J. Virol. 84 (22), 11831–11840.
Stallknecht, D.E., Shane, S.M., Kearney, M.T., Zwank, P.J., 1990. Persistence of avian influenza viruses in water. Avian Dis. 406–411.
Stallknecht, D.E., Goekjian, V.H., Wilcox, B.R., Poulson, R.L., Brown, J.D., 2010. Avian influenza virus in aquatic habitats: what do we need to learn? Avian Dis. 54 (s1), 461–465.
Sturm-Ramirez, K.M., Ellis, T., Bousfield, B., Bissett, L., Dyrting, K., Rehg, J.E., Poon, L., Guan, Y., Peiris, M., Webster, R.G., 2004. Reemerging H5N1 influenza viruses in Hong Kong in 2002 are highly pathogenic to ducks. J. Virol. 78 (9), 4892–4901.
Suarez, D.L., Senne, D.A., 2000. Sequence analysis of related low-pathogenic and highly pathogenic H5N2 avian influenza isolates from United States live bird markets and poultry farms from 1983 to 1989. Avian Dis. 356–364.
Swayne, D.E., 2008. High pathogenicity avian influenza in the Americas. In: Swayne, D.E. (Ed.), Avian Influenza. Wiley-Blackwell, Ames, Iowa, pp. 191–216.
Swayne, D.E., Hill, R.E., Clifford, J., 2017. Safe application of regionalization for trade in poultry and poultry products during highly pathogenic avian influenza outbreaks in the USA. Avian Pathol. 46, 125–130.
Torchetti, M.K., Killian, M.L., Dusek, R.J., Pedersen, J.C., Hines, N., Bodenstein, B., White, C.L., Ip, H.S., 2015. Novel H5 clade 2.3. 4.4 reassortant (H5N1) virus from a green-winged teal in Washington, USA. Genome Announc. 3 (2), e00195–15.
United States Department of Agriculture, Animal and Plant Health Inspection Service, 2017a. '2014–2015 HPAI outbreak'. Available at: 〈https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian-influenza-disease/defend-the-flock/2014-2015-hpai-outbreak〉 (Last accessed 30 June 2017).
United States Department of Agriculture, Animal and Plant Health Inspection Service, 2017b. 'Avian influenza and wild birds'. Available at: 〈https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian-influenza-disease/defend-the-flock/defend-the-flock-ai-wild-birds〉 (Last accessed 30 June 2017).
United States Department of Agriculture, Animal and Plant Health Inspection Service, 2017c. '2017 highly pathogenic avian influenza'. Available at: 〈https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian-influenza-disease/defend-the-flock/2017-hpai〉 (Last accessed 12 July 2017).
Verhagen, J.H., Herfst, S., Fouchier, R.A., 2015. How a virus travels the world. Science 347 (6222), 616–617.
Wasilenko, J.L., Lee, C.W., Sarmento, L., Spackman, E., Kapczynski, D.R., Suarez, D.L., Pantin-Jackwood, M.J., 2008. NP, PB1, and PB2 viral genes contribute to altered replication of H5N1 avian influenza viruses in chickens. J. Virol. 82 (9), 4544–4553.
Wells, S.J., Kromm, M.M., VanBeusekom, E.T., Sorley, E.J., Sundaram, M.E., VanderWaal, K., Bowers, J.W., Papinaho, P.A., Osterholm, M.T., Bender, J., 2017. Epidemiologic investigation of highly pathogenic H5N2 avian influenza among upper midwest US Turkey Farms, 2015. Avian Dis. 61 (2), 198–204.
Wille, M., Robertson, G.J., Whitney, H., Ojkic, D., Lang, A.S., 2011. Reassortment of American and Eurasian genes in an influenza A virus isolated from a great black-backed gull (*Larus marinus*), a species demonstrated to move between these regions. Arch. Virol. 156 (1), 107–115.
Winker, K., McCracken, K.G., Gibson, D.D., Pruett, C.L., Meier, R., Huettmann, F., Wege, M., Kulikova, I.V., Zhuravlev, Y.N., Perdue, M.L., Spackman, E., Suarez, D.L., Swayne, D.E., 2007. Avian influenza migration from Asia to Alaska. Emerg. Infect. Dis. 13 (4), 547–552.
Winker, K., Gibson, D.D., 2010. The Asia-to-America influx of avian influenza wild bird hosts is large. Avian Dis. 54 (Suppl. 1), 477–482.
Xu, W., Berhane, Y., Dubé, C., Liang, B., Pasick, J., VanDomselaar, G., Alexandersen, S., 2016. Epidemiological and evolutionary inference of the transmission network of the 2014 highly pathogenic avian influenza H5N2 outbreak in British Columbia, Canada. Sci. Rep. 6.
Xu, Y., Ramey, A.M., Bowman, A.S., DeLiberto, T.J., Killian, M.L., Krauss, S., Nolting, J.M., Torchetti, M.K., Reeves, A.B., Webby, R.J., Stallknecht, D.E., 2017. Low-pathogenic influenza A viruses in North American diving ducks contribute to the emergence of a novel highly pathogenic influenza A (H7N8) virus. J. Virol. 91 (9), e02208–e02216.