REVIEW

Global Patterns of Influenza A Virus in Wild Birds

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The outbreak of highly pathogenic avian influenza of the H5N1 subtype in Asia, which has subsequently spread to Russia, the Middle East, Europe, and Africa, has put increased focus on the role of wild birds in the persistence of influenza viruses. The ecology, epidemiology, genetics, and evolution of pathogens cannot be fully understood without taking into account the ecology of their hosts. Here, we review our current knowledge on global patterns of influenza virus infections in wild birds, discuss these patterns in the context of host ecology and in particular birds' behavior, and identify some important gaps in our current knowledge.

Influenza A viruses have been isolated from many species, including humans, pigs, horses, mink, felids, marine mammals, and a wide range of domestic birds, but wildfowl and shorebirds are thought to form the virus reservoir in nature. The influenza A virus genome consists of eight segments of negative-stranded RNA, which code for 11 proteins. Influenza viruses are classified on the basis of two of these proteins expressed on the surface of virus particles; the hemagglutinin (HA) and neuraminidase (NA) glycoproteins (*1*). In wild birds and poultry throughout the world, influenza viruses representing 16 HA and 9 NA antigenic subtypes have been detected (*2*), which can be found in numerous combinations (also called subtypes, e.g., H1N1, H16N3).

The HA protein is initially synthesized as a single polypeptide precursor (HA0), which is cleaved into HA_1 and HA_2 subunits by proteases. The mature protein mediates binding of the virus to host cells, followed by fusion with endosomal membranes (*1*). Influenza viruses of subtypes H5 and H7, but not other HA subtypes, may become highly pathogenic after introduction into poultry and can cause outbreaks of highly pathogenic avian influenza (HPAI, formerly termed "fowl plague"). The switch from a low pathogenic avian influenza (LPAI) virus phenotype, common in wild birds and poultry, to the HPAI virus phenotype is achieved by the introduction of basic amino acid residues into the HA0 cleavage site, which facilitates systemic virus replication. HPAI isolates have been obtained primarily from commercially raised poultry (*3*).

In the past decade, HPAI outbreaks have occurred frequently, caused by influenza viruses of subtype H5N1 in Asia, Russia, the Middle East, Europe, and Africa (ongoing since 1997); H5N2 in Mexico (1994), Italy (1997), and Texas (2004); H7N1 in Italy (1999); H7N3 in Australia (1994), Pakistan (1994), Chile (2002), and Canada (2003); H7N4 in Australia (1997); and H7N7 in the Netherlands (2003) (*3*, *4*).

Migratory Birds as a Natural Reservoir of LPAI Viruses

LPAI viruses have been isolated from at least 105 wild bird species of 26 different families (Table 1) (*5*). All influenza virus subtypes and most HA/NA combinations have been detected in the bird reservoir and poultry, whereas relatively few have been detected in other species. Although many wild bird species may harbor influenza viruses, birds of wetlands and aquatic environments such as the Anseriformes (particularly ducks, geese, and swans) and Charadriiformes (particularly gulls, terns, and waders) constitute the major natural LPAI virus reservoir (*1*). Anseriformes and Charadriiformes are distributed globally, except for the most arid regions of the world (*6*).

In birds, LPAI viruses preferentially infect cells lining the intestinal tract and are excreted in high concentrations in their feces. It has been shown that influenza viruses remain infectious in lake water up to 4 days at 22°C and more than 30 days at 0°C (*7*), and the relatively high virus prevalence in birds living in aquatic environments may be due in part to efficient transmission through the fecal-oral route via surface waters (*1*, *7*).

Migration is a common strategy for birds occupying seasonal habitats and may range from short local movements to intercontinental migrations. Migratory birds can carry pathogens, particularly those that do not significantly affect the birds' health status and consequently interfere with migration. Many Anseriformes and Charadriiformes are known to perform regular long-distance migrations (*6*), thereby potentially distributing LPAI viruses between countries or even continents. Birds breeding in one geographic region often follow similar migratory flyways, e.g., the East Asian–Australian flyway from eastern Siberia south to eastern Asia and Australia (Fig. 1A). However, the major flyways are simplifications, and there are numerous exceptions where populations behave differently from the common patterns (*6*, *8*). Within the large continents and along the major flyways, migration connects many bird populations in time and space, either at common breeding areas, during migration, or at shared nonbreeding areas (Fig. 1). As a result, virus-infected birds can transmit their pathogens to other populations that subsequently may bring the viruses to new areas.

It is important to realize that the transmission of the viruses and their geographical spread is dependent on the ecology of the migrating hosts. For instance, migrating birds rarely fly the full distance between breeding and nonbreeding areas without stopping over and "refueling" along the way. Rather, birds make frequent stopovers during migration and spend more time eating and preparing for migration than actively performing flights (*9*). Many species aggregate at favorable stopover or wintering sites, resulting in high local densities. Such sites may be important for transmission of LPAI viruses between wild and captive birds and between different species.

Influenza Viruses in Ducks

Extensive surveillance studies of wild ducks in the Northern Hemisphere have revealed high LPAI virus prevalence primarily in juvenile—presumably immunologically naïve—birds with a peak in early fall before southbound migration. In North America, the prevalence falls from ~60% in ducks sampled at marshalling sites close to the Canadian breeding areas in early fall, to 0.4 to 2% at the wintering grounds in the southern U.S.A., and ~0.25% on the ducks' return to the breeding grounds in spring. Similar patterns have been observed in Northern Europe, but influenza virus detection during spring migration can be significantly higher, up to 6.5%. Surveillance of the nesting grounds of ducks in Siberia before winter migration revealed the presence of influenza viruses in up to 8% of birds (*10*).

Such year-round prevalence raises the possibility that LPAI virus can persist in ducks alone. This hypothesis complements earlier ones, in which additional host species or preservation of infectious influenza viruses in frozen lakes over the winter play a role in the perpetuation of avian influenza viruses (*1*, *7*).

All HA and NA subtypes, with the exception of H13 to H16, circulate in wild ducks in North America and Northern Europe. In a 26-year longitudinal study performed in Canada, influenza viruses of subtypes H3, H4, and H6 were isolated from ducks most frequently; H1, H2, H7, H10,

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and H11 less frequently; and H5, H8, H9, and H12 only sporadically. Although in other North American and European studies, influenza viruses of subtypes H3, H4, and H6 were also detected frequently, the detection of other virus subtypes was not significantly different (*4*, *11*). Thus, the prevalence of influenza virus in general, as well as the specific distribution of subtypes, may vary between different surveillance studies depending on species, time, and place.

In the Canadian studies, cyclic patterns of influenza virus subtypes were reported: Peaks in virus isolation of an HA subtype were followed 1 to 2 years later by reduced rates of isolation of this subtype. This observation awaits confirmation in other surveillance studies but is of particular interest in relation to findings for other infectious diseases: Cyclic patterns described for measles and whooping cough in humans have provided new insights in the role of spatial factors, herd immunity, and population age-structure on epidemiology (*12*). Cycling of influenza virus in wild birds could provide similar new insights into the ecology of influenza viruses in their natural hosts.

Influenza virus surveillance of ducks has been performed in Japan since the late 1970s. As in other studies, influenza virus prevalence and isolated subtypes varied between years and locations (*5*). The prevalence of influenza virus in wild birds elsewhere in Asia is largely unknown, but several studies have been conducted in live bird markets, where most HA and NA subtypes were found in poultry (*1*, *13*). It is plausible that the circulation of the LPAI virus subtypes in poultry at least partially reflects that in wild birds, but no direct connection has yet been established.

Dabbling ducks of the *Anas* genus, with Mallards (*Anas platyrhynchos*) as the most extensively studied species, have been found to be infected with influenza viruses more frequently than other birds, including diving ducks (Table 1) (*5*). Differences in virus prevalence between ecological guilds of ducks are likely in part related to behavior. Dabbling ducks feed primarily on food in surface waters; diving ducks forage at deeper depths and more often in marine habitats (*6*). Dabbling ducks display a propensity for abmigration, the switching of breeding grounds between years, which is in part due to mate choice (*6*). This behavior could provide an opportunity for influenza viruses to be transmitted between different host subpopulations. LPAI virus infection generally causes no major clinical signs in dabbling ducks, and experimental infections indicate that animals only produce a transient, low-level humoral immune response, which may be sufficient to provide partial protection against reinfection with viruses of the same subtype but is unlikely to confer protection against heterologous reinfections (*14*). Different influenza virus subtypes can also infect ducks concomitantly, creating the opportunity for genetic mixing (*15*).

Table 1. Prevalence of influenza A virus in wild birds. Influenza virus prevalence in specific species is given only if tests on >500 birds have been reported; lower numbers in individual species are included in the total. See (*5*) for additional comments and original data. Of the 36 species of ducks, 28,955 were dabbling ducks and 1011 were diving ducks, with influenza virus prevalence of 10.1 and 1.6%, respectively.

Family	Species	Sampled	Positive	
			(*n*)	(%)
Ducks	36 species	34,503	3275	9.5
	Mallard (*Anas platyrhynchos*)	15,250	1965	12.9
	Northern Pintail (*Anas acuta*)	3,036	340	11.2
	Blue-winged Teal (*Anas discors*)	1,914	220	11.5
	Common Teal (*Anas crecca*)	1,314	52	4.0
	Eurasian Wigeon (*Anas penelope*)	1,023	8	0.8
	Wood Duck (*Aix sponsa*)	926	20	2.2
	Common Shelduck (*Tadorna tadorna*)	881	57	6.5
	American Black Duck (*Anas rubripes*)	717	130	18.1
	Green-winged Teal (*Anas carolinensis*)	707	28	4.0
	Gadwall (*Anas strepera*)	687	10	1.5
	Spot-billed Duck (*Anas poecilorhyncha*)	574	21	3.7
Geese	8 species	4,806	47	1.0
	Canada Goose (*Branta canadensis*)	2,273	19	0.8
	Greylag Goose (*Anser anser*)	977	11	1.1
	White-fronted Goose (*Anser albifrons*)	596	13	2.2
Swans	3 species	5,009	94	1.9
	Tundra Swan (*Cygnus columbianus*)	2,137	60	2.8
	Mute Swan (*Cygnus olor*)	1,597	20	1.3
	Whooping Swan (*Cygnus cygnus*)	930	14	1.5
Gulls	9 species	14,505	199	1.4
	Ring-billed gull (*Larus delawarensis*)	6,966	136	2.0
	Black-tailed Gull (*Larus crassirostris*)	1,726	17	1.0
	Black-headed Gull (*Larus ridibundus*)	770	17	2.2
	Herring Gull (*Larus argentatus*)	768	11	1.4
	Mew Gull (*Larus canus*)	595	0	0.0
Terns	9 species	2,521	24	0.9
	Common Tern (*Sterna hirundo*)	961	16	1.7
Waders	10 species	2,637	21	0.8
Rails	3 species	1,962	27	1.4
	Eurasian Coot (*Fulica atra*)	1,861	23	1.2
Petrels	5 species	1,416	4	0.3
	Wedge-tailed Shearwater (*Puffinus pacificus*)	794	4	0.5
Cormorants	1 species	4,500	18	0.4
	Great Cormorant (*Phalacrocorax carbo*)	4,500	18	0.4

Little is known about the prevalence of influenza viruses in wild ducks in the Southern Hemisphere or potential transmission between the hemispheres. There is little connectivity between northern and southern Anatidae species, and most species stay year round within each breeding continent. The Blue-winged Teal (*Anas discors*) is one of the few North American species that has a winter distribution that includes South America (Fig. 1C) (*6*). There are several other duck species that could serve as hosts for influenza virus in South America (*6*), but surveillance data are not available. Similarly, only 6 of 39 Anatidae species breeding in Eurasia winter with at least part of the population south of the Sahara desert in Africa, e.g., the Garganey (*Anas querquedula*) (Fig. 1C) and the Northern Pintail *(Anas acuta)*, each have African winter populations in excess of one million birds (*16*). As in South America, none of the 22 Anatidae species that breed in sub-Saharan Africa spend the nonbreeding season outside the continent. However, there are several species with large, widespread populations in Africa (*16*), and some migrate within Africa (*17*). Potential areas for mixing of Eurasian and African ducks are in West Africa, near the Senegal and Niger Rivers, the floodplains of the Niger River in Nigeria and Mali, and Lake Chad (*16*), and influenza viruses in African Anatidae populations may thus be linked to Eurasia through migrating species. Anatidae of Oceania are mainly resident and do not perform regular seasonal migrations (*6*).

Influenza Viruses in Gulls and Terns

The first recorded isolation of influenza virus from wild birds was from a Common Tern (*Sterna*

hirundo) in 1961. This HPAI H5N3 virus was responsible for an outbreak in South Africa where at least 1300 of these birds died (*3*). The most frequently detected LPAI virus subtype in gulls is H13, a subtype rarely found in other birds. Recently, a "novel" virus subtype (H16), related to H13, was described in Black-headed Gulls (*Larus ridibundus*) in Sweden. The genes of H13 and H16 viruses are genetically distinct from those of influenza viruses from other hosts, which suggests they have been genetically isolated for sufficient time to allow genetic differentiation (*2*). This concurs with the observation that gull influenza viruses do not readily infect ducks when they are inoculated experimentally (*1*). Although other influenza virus subtypes are also occasionally detected in terns and gulls (Table 1) (*5*), it is plausible that the viruses that are genetically indistinguishable from viruses of other avian hosts are most likely not endemic in gulls and terns.

Influenza viruses can be detected in a small proportion of gulls, with the highest virus prevalence reported in late summer and early fall. Most gull species breed in colonies (*6*), with adults and juveniles crowded in a small space, creating good opportunities for virus spread. This situation contrasts with that in dabbling ducks that do not breed in dense colonies (*6*), and epizootics could be more easily initiated when birds congregate in large numbers during molt, migration, or wintering.

Influenza Viruses in Waders

Waders in the Charadriidae and Scolopacidae families are adapted to either marine or freshwater wetland areas and often live side-by-side with ducks (*18*). Long-term influenza virus surveillance studies are still sparse, but data from North America suggest a distinct role of these birds in the perpetuation of certain virus subtypes. Influenza viruses of subtypes H1 to H12 have been isolated in birds migrating through the eastern U.S.A., with a high prevalence of certain HA subtypes (H1, H2, H5, H7, H9 to H12) and a larger variety of HA/NA combinations as compared with ducks in Canada, suggesting that waders maintain a wider spectrum of viruses. Moreover, the seasonal prevalence of influenza viruses in waders seems to be reversed as compared with ducks, with higher virus prevalence (~14%) during spring migration (*19*). This has led to the hypothesis that different families of wetland birds are involved in perpetuation of LPAI virus and suggests a role for waders, which may carry the virus north to the duck breeding grounds in spring. Recent genetic analyses have not revealed striking differences between influenza viruses from ducks and waders in the Americas, suggesting that these viral gene pools are not separated (*20*, *21*). Although the wader-duck link may be a plausible scenario based on the North American data, studies in waders in Northern Europe have failed to produce similar results. Nevertheless, many wader species of the Northern Hemisphere are long-distance intercontinental migrants (*8*) and may, therefore, have the potential to distribute influenza viruses around the globe.

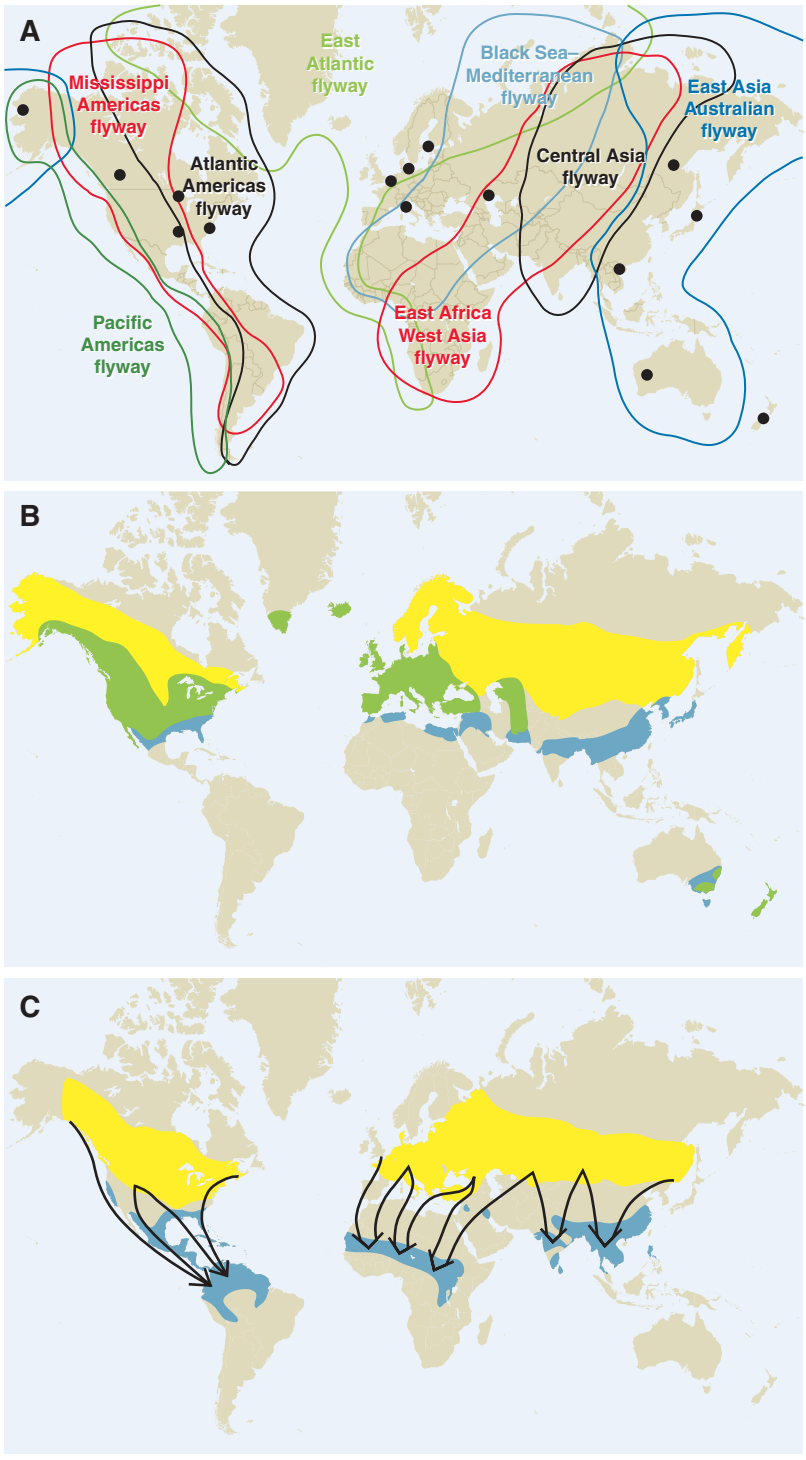

Fig. 1. Migratory flyways of wild bird populations. A world map with the main general migratory flyways of wild bird populations is shown (adapted from information collected and analyzed by Wetlands International). (**A**) Black dots indicate the locations of historical and current influenza virus surveillance sites from which data have been used in this manuscript. These global migration flyways are simplifications, and there are situations where populations behave differently from the common patterns. Migration patterns of Mallard (*Anas platyrhynchos*) (**B**) and Garganey (*Anas querquedula*) in Eurasia and Africa and Blue-winged Teal (*Anas discors*) in the Americas (**C**) (right and left parts of the map, respectively) are provided. Yellow color indicates breeding areas in which species are absent during winter, green indicates areas in which species are present around the year, and blue indicates areas in which species are only present in winter and do not breed. Arrows indicate the seasonal migration patterns.

Influenza Viruses in Other Wild Birds

LPAI viruses can be found in numerous other bird species (Table 1) (*5*), but it is unclear in which of these species influenza viruses are endemic and in which the virus is a temporary pathogen. Species in which influenza viruses are endemic share the same habitat at least part of the year with other species in which influenza viruses are frequently detected, including geese, swans, rails, petrels, and cor-

morants. In these birds and others (*5*), influenza virus prevalence seems to be lower than in dabbling ducks (Table 1), but it should be noted that studies on these species are limited, and it is possible that peak prevalence has been missed because of its seasonal nature or location.

As for ducks, gulls, and waders, their behavior and ecology may be an important determinant of their role as host species. For instance, geese are mainly herbivorous and often congregate in large flocks for grazing in pastures and agricultural fields, especially during the nonbreeding season. Such flocks may reach tens of thousands of birds in optimal areas and often contain several different species. Colonial breeding occurs in some goose species, but most are solitary nesters or nest in loose groups with little interaction between pairs. Given that wild geese and ducks are the ancestors of today's domestic goose and duck species and that these domestic animals in parts of the world are frequently kept alongside chickens, wild geese and ducks may form the bridge for influenza viruses between wild and domestic birds.

Genetic Variation of Influenza Viruses in Wild Birds

Evolution of avian influenza viruses in their natural hosts is slow, but not negligible. Avian influenza viruses can be divided into two lineages, Eurasian and American (Fig. 2), probably as a result of long-term ecological and geographical separation of hosts. However, the avifauna of North America and Eurasia are not completely separated; some ducks and shorebirds cross the Bering Strait during migration or have breeding ranges that include both the Russian Far East and northwestern North America (*6*). The majority of tundra shorebirds from the Russian Far East winter in Southeast Asia and Australia, but some species winter along the west coast of the Americas (*22*). The overlap in distribution of ducks is not as profound as that of shorebirds, but a few species (e.g., Northern Pintail, *Anas acuta*) are common in both North America and Eurasia (*6*) and could also provide an intercontinental bridge for influenza virus. Indeed, influenza viruses carrying a mix of genes from the American and Eurasian lineages have been isolated, indicating that allopatric speciation is only partial (*23*–*25*). The partial ecological isolation of influenza virus hosts seems sufficient to facilitate divergent evolution of separate gene pools, but allows occasional spillover of gene segments from one gene pool to the other.

Within each genetic lineage, multiple sublineages of viral genes cocirculate, but there appear to be no consistent temporal or spatial correlations. Moreover, genetic data from duck and shorebird influenza virus isolates from the Americas suggest an active interplay between these host species (*20*, *21*). Although certain HA subtypes are reported to be more prevalent in either shorebirds or ducks in North America, this also does not seem to have resulted in differences in the genetic composition of influenza viruses obtained from these two reservoirs (*19*, *26*).

The segmented nature of the influenza virus genome enables evolution by a process known as genetic reassortment, i.e., the mixing of genes from two or more influenza viruses. A recent study of 35 influenza virus isolates obtained from ducks in Canada indicates that genetic "sublineages" do not persist, but frequently reassort with other viruses (*27*). Influenza viruses of a particular subtype do not necessarily have the same genetic make-up, even within a single year or a single host species. The high prevalence of influenza virus in some wild bird species and the sporadic detection of concomitant infections in single birds (*15*) support the notion that reassortment may occur in nature. Gaining information on the actual frequency of reassortment in the wild bird reservoir and the impact of these events on LPAI virus evolution will be of considerable interest.

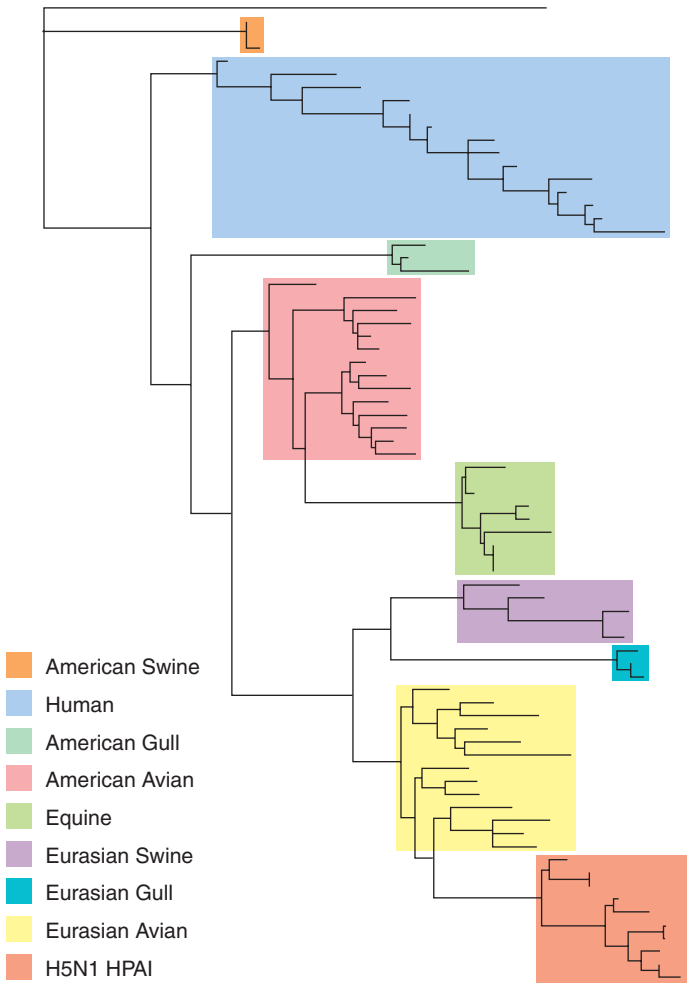

Fig. 2. Phylogenetic tree for the matrix gene of influenza A viruses from a variety of hosts. Nucleotide sequences were selected from public databases and aligned, after which a maximum likelihood tree was generated using influenza virus A/Equine/Prague/57 (H7N7) as outgroup. Sequences were selected from each host to reflect the longest possible time frame and variation in locations of virus isolation. The avian influenza viruses are divided in an American lineage (pink) and a Eurasian lineage (yellow), and there are no clear patterns of host, temporal, or spatial correlation within these lineages. In contrast, the human influenza A virus lineage (light blue), the Eurasian swine lineage (purple), and the HPAI H5N1 lineage (orange) display clear temporal patterns of virus evolution.

HPAI H5N1 Viruses in Wild Birds

In 1997, an HPAI outbreak caused by H5N1 influenza virus occurred in chicken farms and the live bird markets of Hong Kong, which also resulted in the first reported case of human influenza and fatality attributable directly to avian influenza virus (*28*). The H5N1 HPAI virus reappeared in 2002 in waterfowl at two parks in Hong Kong and was also detected in other captive and wild birds (*29*). It resurfaced again in 2003 and has devastated the poultry industry in large parts of Southeast Asia since 2004. In 2005, the virus was isolated during an outbreak among migratory birds in Qinghai Lake, China, affecting large numbers of wild birds (*30*). This single epizootic caused an estimated 10% decrease of the global population of Bar-headed Geese (*Anser indicus*), highlighting the potential devastating effects on vulnerable wildlife. Subsequently, the virus has appeared across Asia, Europe and the Middle East, and in several African countries. Wild bird deaths have been reported in several of these countries, in Europe, particularly affecting Mute Swans (*Cygnus olor*) and Whooper Swans (*Cygnus cygnus*), but mortality has also been recorded in other waterfowl species, and occasionally in raptors, gulls, and herons. So far, the HPAI H5N1 strain that originated in poultry in Southeast Asia has caused mortality in >60 wild bird species (*29*–*31*). In addition, during the devastating outbreaks in poultry, the H5N1 virus was transmitted to 175 humans, leading to 95 deaths (as of 6 March 2006), and has also

been isolated from pigs, cats, tigers, and leopards.

It is most likely that the H5N1 virus has circulated continuously in domestic birds in Southeast Asia since 1997 and, as a consequence, has evolved substantially (Fig. 2). Surveillance studies in Mainland China from 1999 onward indicated that H5N1 viruses have become endemic in domestic birds in the region and that multiple genetic lineages of the virus are cocirculating (*32*, *33*). Poultry trade and mechanical movement of infected materials are likely modes for spreading HPAI in general (*3*). For the H5N1 virus, it is without doubt that domestic waterfowl, specific farming practices, and agroecological environments played a key role in the occurrence, maintenance, and spread of HPAI for many affected countries (*34*, *35*). Although numerous wild birds have also become infected, it has been much debated whether they play an active role in the geographic spread of the disease. It has been argued that infected birds would be too severely affected to continue migration and thus unlikely to spread the H5N1 virus. Although this may be true for some wild birds, it has been shown that, in experimental infections, several bird species survive infection and shed the H5N1 virus without apparent disease signs (*31*, *32*, *36*). In addition, many wild birds may be partially immune owing to previous exposures to LPAI influenza viruses, as has been shown for chickens (*37*). Finally, recent studies suggest that HPAI viruses may become less pathogenic to ducks infected experimentally, while retaining high pathogenicity for chickens (*32*, *36*, *38*). The present situation in Europe, where infected wild birds have been found in several countries that have not reported outbreaks among poultry, suggests that wild birds can indeed carry the virus to previously unaffected areas. Although swan deaths have been the first indicator for the presence of the H5N1 virus in several European countries, this does not necessarily imply a role as predominant vectors; they could merely have functioned as sentinel birds infected via other migrating bird species.

Prospects

Despite the relatively intense surveillance studies that have been performed for many years in North America and Eurasia, our understanding of the global distribution of LPAI viruses in wild bird populations is still limited. Serological evidence indicates that influenza viruses occasionally circulate in Antarctica (*39*), and it is reasonable to assume that influenza viruses are distributed globally, wherever competent host species are present. It is possible that some subtypes are rare or not detected annually in current surveillance studies. Simply because of the limitations of our studies, we are currently biased toward species that are easy to sample during migration or wintering. Second, to understand the global patterns of LPAI viruses in wild birds, it will be crucial to integrate virus and host ecology with long-term surveillance studies to provide more insight on the year-round perpetuation of influenza viruses in wild birds. Possible intercontinental contacts among ducks and shorebirds in areas where migrating birds from the northern and southern latitudes mix are of particular interest. Can influenza viruses be perpetuated in ducks alone, or does the interface between ducks and shorebirds, as seems to occur in North America (*19*), also occur on other continents? With high-throughput sequencing technology, it should be possible to gain more insight into the genetic variability and evolution of LPAI viruses in wild birds and to integrate this information with epidemiology and virus-host ecology.

The recent H5N1 outbreaks in Eurasia have identified additional gaps in our knowledge of avian influenza viruses in wild birds in general. It should be realized that our knowledge of LPAI viruses in wild birds cannot simply be extrapolated to HPAI viruses; for instance, the most important host species or routes of transmission may be quite different (Table 1) (*29*–*31*, *38*). It is clear that influenza virus surveillance of wild birds could provide "early warning" signals for the introduction of HPAI H5N1 virus in new regions and may provide access to strains for characterization. For proper risk assessment studies, however, we also need a better understanding of the interface between wild and domestic birds, the possible transmission of influenza viruses between these populations, bird behavior, age-structures of populations, and detailed migration routes. We further need better understanding of the transmission and pathogenesis of H5N1 virus in wild birds, as well as identification of virus-permissive host species and their relative likelihood to develop disease, patterns of virus secretion, and temporal and spatial variations in virus prevalence.

With our current limited knowledge on HPAI in wild birds, there is no solid basis for including wild birds in control strategies beyond the physical separation of poultry from wild birds. Even in areas with significant outbreaks in poultry, virus prevalence in wild birds is low (*32*), and the role of these wild birds in spreading the disease is unclear. It is clear that the H5N1 problem originated from outbreaks in poultry and that the outbreaks and their geographical spread probably cannot be stopped without implementation of proper control measures in the global poultry industry. However, there is at present no scientific basis for culling wild birds to control the outbreaks and their spread, and this is further highly undesirable from a conservationist perspective.

The current increased interest in influenza virus surveillance in wild and domestic birds provides a unique opportunity to increase our understanding not only of HPAI epidemiology but also of the ecology of LPAI viruses in their natural hosts, at the same time and for the same cost.

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Supporting Online Material

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Table S1
References and Notes

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