By Colin A. Russell

In 2014, a new, highly pathogenic avian influenza virus (HPAIV) called H5N8 caused outbreaks in poultry in East and Southeast Asia and spread across the Northern Hemisphere to Europe and North America. In the United States alone, H5N8 outbreaks resulted in the destruction of more than 48 million poultry birds (1). International live-poultry trade and wild-bird migration have both been implicated in the intercontinental movement of H5N8 and other HPAIVs. H5N8 viruses have been found in wild birds (2–4), but strong links between poultry outbreaks and live-poultry trade or wild-bird migration have been elusive. On page 213 of this issue, the Global Consortium for H5N8 and Related Influenza Viruses (5) delineates the contributions of live-poultry trade and wild-bird migration to the global spread of H5N8 viruses.

Live-poultry trade and wild-bird migration are both plausible mechanisms for the global movement of HPAIVs. The world’s poultry population exceeds 50 billion animals, and the global network of live-poultry trade is extensive. Furthermore, HPAIVs are most commonly found in, and are thought to originate from, poultry (6). Although HPAIVs are less often found in wild birds, they have been collected from various wild-bird species, and wild birds are the natural reservoir of all avian influenza virus subtypes. Wild-bird migration has the potential to move viruses long distances and introduce them to new populations, particularly where migratory flyways overlap (see the figure) (6, 7).

To investigate the spread of H5N8 viruses, the Global Consortium combined analyses of epidemiological, genetic, and ornithological data from Asia, Europe, and North America. These data consistently point to a prominent role of wild birds in spreading the viruses from Asia into Europe and North America via circumpolar migratory flyways (see the figure). In contrast, international trade data from the Food and Agriculture Organization...
Trumpeter and tundra swans rest at Marsh Lake during their spring migration north through the Yukon Territory, Canada.

(FAO) argue strongly against live-poultry trade as the mechanism of international H5N8 virus spread from Asia. Data for 2011 show that East and Southeast Asia is overwhelmingly a net importer of live chickens and ducks from Europe and North America, with no reported exports to Europe or North America (8). These data do not, however, account for undocumented poultry trade, which could be an important vehicle for the global spread of other HPAIVs or potential future recurrences of H5N8 viruses.

A fundamental question about the H5N8 viruses is why they spread intercontinentally, whereas most other HPAIVs have not. The answers are likely to be pathological, virological, and ecological.

One hypothesis against wild birds spreading HPAIVs is based on the adage that sick birds do not fly. Birds on the brink of death are unlikely to migrate, but mild-to-moderate infections might be only minor impediments to flight. In a recent experimental study of mallard ducks, many HPAIVs caused little or no illness, whereas H5N8 viruses caused moderate disease (9). H5N8-infected mallards shed virus at higher titers than birds infected with other viruses, indicating increased onward transmission potential.

H5N8 viruses have been isolated from apparently healthy wild birds (10), suggesting that some infected birds could migrate without being hindered by illness.

Additional questions remain about the H5N8 virus. The H5N8 hemagglutinin protein reassorts more frequently with the neuraminidase proteins from other influenza viruses than do other H5 virus hemagglutinins. Combined with the rapid spread of the H5N8 virus, the ability of this hemagglutinin to readily pair with proteins from different viruses implies high fitness. However, the biological underpinnings for this fitness are unexplained. Similarly, despite spreading efficiently among wild birds in North America, H5N8 viruses have not been detected there since mid-2015, and this apparent extinction is not understood (11).

Host ecology also plays an important role in the spread of human (12) and animal (6) pathogens. For HPAIVs, a critical step for intercontinental spread is getting into a mobile population. In poultry, viruses must get into populations that will be exported. Timing of introduction relative to export is critical because onward transmission requires that birds still be infectious upon arrival. In wild birds, viruses must get into migratory species that can migrate after infection. As the Global Consortium shows, infecting species prone to long-distance migration is particularly important.

The risks posed by HPAIVs require that we attempt to mitigate their spread. Improving surveillance is an oft-repeated solution but is fraught with challenges. Enhancing surveillance in wild birds where migratory flyways overlap, particularly the Arctic, could provide an early-warning system for the spread of new viruses. However, these overlaps cover huge geographic areas (see the figure) and involve enormous wild-bird populations, each with its own complex ecology. For poultry, any sufficiently large population has the potential to harbor influenza viruses of concern for animal and human health. We urgently require detailed assessments of where surveillance is most needed and could have the greatest impact.

We also require effective and economically viable protocols for when and how to react to surveillance data, particularly from wild birds. Underreacting to surveillance data costs animal lives and money and devalues surveillance efforts. Overreacting costs money and breeds mistrust, as does continuing to react once a threat has passed. Detection of HPAIVs in migratory wild birds should trigger increased biosecurity on poultry farms rather than actions against wild birds: Wild-bird populations are too large and HPAIVs spread too quickly for strategies like wild-bird culling to be effective.

Development of global wild-bird and poultry surveillance systems that can provide actionable information in real time will require a globally unified reporting infrastructure and dramatic increases in funding. However, huge progress could be realized for a fraction of the economic cost of the H5N8 outbreaks in the United States, which cost more than US$3.3 billion (1) and could aid control of other pathogens. We must remember that surveillance is a process rather than a goal and thus requires stable, long-term financial support. After all, the threats posed by avian influenza viruses do not fluctuate according to research or government funding cycles.

**REFERENCES**