Despite treatment, this bald eagle in Wisconsin became one of many wild birds killed by avian flu.

PHOTO: WISCONSIN HUMANE SOCIETY

INFECTIOUS DISEASE

Deadly flu spreads through North American birds

As largest ever H5N1 outbreak hits poultry and wild species, researchers wonder whether virus is here to stay

By **Erik Stokstad**

When black vultures began to die at Florida's Hontoon Island State Park in February, rangers called in investigators from the state's Fish and Wildlife Conservation Commission. They soon concluded a virus that has devastated domesticated birds worldwide had reached the vultures: a strain of highly pathogenic avian influenza (HPAI) known as H5N1. The vultures had likely acquired the virus from eating infected waterbirds—as well as by cannibalizing their own kind.

Workers removed more than 200 carcasses in a bid to contain the outbreak. But Mark Cunningham, a wildlife veterinarian with the commission, thinks the effort was probably futile. "It's hard to see this chain of infection really breaking anytime soon," he says.

That's a fear shared by researchers and poultry farmers across North America, who in recent weeks have been urgently documenting and trying to contain the continent's largest outbreak of HPAI (p. 459). Since the virus was first spotted in eastern Canada in November 2021, it has been spreading across the continent with migrating waterfowl (see map, p. 442). Poultry farmers have killed nearly 33 million chickens and turkeys in a bid to save other flocks and curb economic losses. Meanwhile, the virus has killed an untold number of wild birds; researchers have so far documented infections in 51 species, including bald eagles and great horned owls. That's more than twice the number of species known to have been infected during the last North American HPAI outbreak, in 2014–15.

HPAI can be far deadlier to birds than seasonal flus are to people, and each outbreak stirs fears about human infection. The current wave has produced no known human cases in North America, however, much to the relief of public health experts already battling COVID-19.

Still, the scope of the HPAI outbreak "boggles the mind," says disease ecologist Nichola Hill of the University of Massachusetts, Boston. She's one of many researchers scrambling to understand how the virus might spread to mammals and whether it will hang on indefinitely in North America, as it has in Europe and Asia. "It's everyone on board, at max capacity," says Susan Shriner, an ornithologist at the U.S. Department of Agriculture, which is helping coordinate the research effort.

The most important HPAI lineage, part of the H5 group of viruses, arose in the late 1990s in domestic geese in Asia. Soon it reassorted with flu strains found in wild waterbirds. In poultry, infections cause pneumonia, seizures, and hemorrhaging with mortality rates of up to 100%. Further mutations enabled those early waves of H5 viruses to infect people—H5N1 has killed 456 since 2003—raising fears that the viruses could cause a pandemic. But so far, they have not gained the ability to readily spread from person to person.

The H5 viruses did, however, cause catastrophic losses of poultry in Southeast Asia. And migratory birds carried the H5N1 strain out of Asia, first to Europe, where it killed an array of water birds, predatory birds, and scavengers such as buzzards. During the earliest outbreaks, the risk was highest during peak fall migration, when waterfowl arrived in Europe. But in the past 2 years, the virus has become endemic in Europe, present at some level year-round in wild birds. The virus "is not something that is going to go away anytime soon," says Arjan Stegeman, a veterinary epidemiologist at Utrecht University.

Because of the persistence of the virus—and the emergence of an apparently more pathogenic strain of H5N1—Europe has been experiencing ever-worsening HPAI outbreaks in both domestic and wild flocks. Farmers have had to undertake massive culls, and producers of free-range poultry have been forced to move their flocks indoors. Sixty-two wild species have been found infected in Europe and the Middle East in the past 4 months, with some—including barnacle geese, Dalmatian pelicans, and common cranes in Israel—suffering worrisome losses.

In North America, officials have been keeping a wary eye on H5N1. In 2014, migrating birds brought a related virus, H5N8, from Asia to the U.S Pacific Northwest, sparking an outbreak that ultimately caused U.S. farmers in 15 states to kill some 50 million chickens and turkeys and tally $3 billion in losses. This time, H5N1 appears to have arrived from Europe. Last year, after surveys found the strain circulating at high levels among wild birds in Western Europe, U.S.

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officials increased their vigilance and requested funds to sample more waterbirds killed by hunters along the Atlantic and Pacific flyways.

In December 2021, several hundred birds died at a petting farm in Newfoundland and tested positive. The next month tests showed a duck killed by a hunter in South Carolina was carrying H5N1. By February, the virus had reached the confluence of the Ohio and Mississippi rivers, where the first farm reported an infection. Since then, migratory birds have spread the virus into the Missouri River Basin and the Great Plains.

Researchers have not yet tested the transmissibility of the virus, but they suspect it spreads more easily than previous strains. That would mean a higher proportion of migratory birds get infected, the geographic spread is wider, and there's a higher prevalence in waterbirds—and hence more spillover into poultry and wild birds, says Bryan Richards, emerging disease coordinator at the U.S. Geological Survey's National Wildlife Health Center.

Genetic analyses of the virus suggest introductions to farms are coming primarily from nearby wild birds. In contrast, researchers believe that during the 2014–15 outbreak of H5N8 humans often accidentally moved the virus from farm to farm.

To prevent infections, many zoos have moved their captive birds indoors or away from visitors. It's much harder to protect wild birds, however, raising fears that the virus could threaten endangered species, especially those with small populations. So far, however, the number of detected infections in wild populations is relatively low, so researchers are "cautiously optimistic ... that we will not see tremendous impacts," Richards says.

Just two songbird species have tested positive: blue jays and crows. At greater risk are water birds, especially those that form dense nesting colonies, and birds that prey on them. Bald eagles often hunt ducks and geese, and some have apparently infected their young by feeding them virus-laden prey, says Rebecca Poulson, a wildlife disease researcher with the Southeastern Cooperative Wildlife Disease Study at the University of Georgia. As of 26 April, 48 eagles known to be infected had died. The eagle deaths—and those of less charismatic birds—are "really heartbreaking," she says. "We've just had our heads hung low some days."

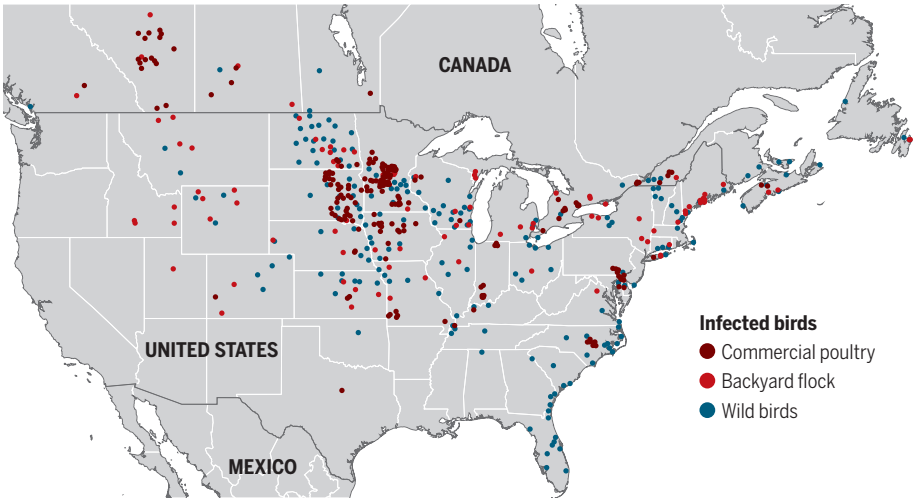
In 2015, Richards says, infections among wild birds petered out in summer as they moved north and dispersed across their nesting grounds, and as lakes and wetlands warmed, creating conditions inhospitable for the virus. This summer, "Knock on wood, we should see a substantial waning of impacts in backyard flocks and commercial operations as well," he says.

But the threat could re-emerge when birds start to migrate south in September. To help farmers stay on guard, the United States will nearly double surveillance efforts. One fear, says Thijs Kuiken, an avian influenza expert at Erasmus University Rotterdam, is that H5N1 will spread south of the U.S. border. Farms there are likely to be more vulnerable.

"People in Central America and South America really need to be aware," he says, "that this virus is likely to arrive on their doorstep—if it hasn't already." ■

A fowl plague

H5N1, a highly pathogenic avian flu virus, arrived from Europe in late 2021. Waterfowl have since spread the virus to other species, including poultry, forcing farmers to kill millions of chickens and turkeys.



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COVID-19

India's speedy vaccine approvals come under fire

Critics say regulatory agency lacks key capabilities and independence

By **Priyanka Pulla**

A COVID-19 vaccine named Corbevax looked like a triumph for India's burgeoning drug industry. Because its U.S. developers hadn't claimed a patent on it, an Indian manufacturer named Biological E was able to sell the two-dose protein-based vaccine to the government at the extraordinarily low price of 145 rupees ($1.90) per dose. In March, the country began to give the shots to 12- to 14-year-olds, a group for which India did not yet have a licensed COVID-19 vaccine.

But the celebration was quickly drowned out by questions over whether India's drug regulator, the Central Drugs Standard Control Organization (CDSCO), had properly vetted the vaccine.

In February, CDSCO had authorized the use of Corbevax for adolescents ages 12 to 18. But within weeks, the Indian media outlet *The Wire Science* revealed that the National Technical Advisory Group on Immunisation (NTAGI), an expert group that advises the health ministry on which vaccines to add to the national immunization program, had questioned whether Biological E had shown the vaccine is effective. In adolescents, who are at a lower risk of severe COVID-19, the benefits of a vaccine should be beyond any doubt, NTAGI member Jayaprakash Muliyil tells *Science*: "Anytime you vaccinate children, you have to be extremely careful."

Other CDSCO approvals of COVID-19 vaccines have raised questions as well, both from NTAGI and independent experts. The agency has used "suboptimal" standards on several occasions, says Vineeta Bal, an immunologist at India's National Institute of Immunology. That has led some scientists to ask whether the agency has the capabilities—and is independent enough—to oversee the quality of medicines for India's 1.4 billion people. The implications go beyond India, because

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