Vigilance Urged Against Bird Flu Amid Ongoing Outbreaks in Mammals

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In one of the latest developments in the ongoing bird flu outbreaks, 28 domestic cats in Poland have tested positive for the highly pathogenic avian influenza A(H5N1) virus, which has decimated global poultry populations, caused mass deaths among wild birds, and infected more than 40 mammalian species.

How the felines were exposed to the virus is under investigation, the World Health Organization (WHO) reported. The cats were located in different areas of Poland, and several had no access to the outdoors, where they might have been exposed to infected animals.

No humans appear to have been infected in Poland’s domestic cat outbreak. In fact, although 900 human infections with H5N1 viruses have been reported globally over the past 3 decades, infections in humans have been rare in the current outbreak, which is dominated by the H5 clade 2.3.4.4b. From January 2022 to June 29, 2023, thirteen A(H5N1) cases in people, including 2 deaths, have been reported globally, according to the US Centers for Disease Control and Prevention (CDC). This July, the UK reported 2 additional cases in asymptomatic poultry workers. Most of the cases have been in people who were in contact with sick or dead infected poultry or contaminated environments, and none were instances of human-to-human transmission.

Still, in a July 12 situation analysis, the WHO, alongside the Food and Agriculture Organization of the United Nations and the World Organisation for Animal Health, warned that the increasing infections in mammals could allow the virus to evolve to infect humans more easily.

In an email to JAMA, Jonathan Runstadler, DVM, PhD, who recently investigated H5N1 avian influenza infections in marine mammals, said he agrees. “The circulation of the H5 2.3.4.4b lineage of virus continues to pose a threat for emerging disease in humans and that is evidenced by continued isolation from both avian and mammalian hosts in minor outbreaks like the situation in the cats,” said Runstadler, who is a professor and chair of the Department of Infectious Disease and Global Health at Tufts University’s Cummings School of Veterinary Medicine.

The WHO and its partners urged nations to take a proactive approach to protect animals, people, and economies from avian influenza. “We encourage all countries to increase their ability to monitor these viruses and to detect any human cases,” Sylvie Briand, MD, MPH, PhD, director of epidemic and pandemic preparedness and prevention at the WHO, said in the recent analysis. “This is especially important as the virus is now affecting countries with limited prior experience in avian flu surveillance.”

Cause for Concern

Throughout the US, more than 7000 wild birds and more than 800 commercial or backyard flocks have tested positive for highly pathogenic avian influenza A(H5) or A(H5N1) virus since January 2022, according to US Department of Agriculture data. Nearly 60 million birds in commercial or backyard flocks have been affected during the outbreak, but no infections in poultry have been detected in the US since mid-May of this year.

A July 7 CDC technical report on highly pathogenic avian influenza A(H5N1) viruses noted that the agency, working with state and local public health departments, has monitored more than 6500 people in the US who were exposed to infected birds and poultry, identifying only 1 infection. That case, in a poultry worker, may have represented contamination with virus RNA in the individual’s upper respiratory specimen rather than true infection, Tim Uyeki, MD, MPH, MPP, chief medical officer of the CDC’s influenza division, explained in an interview with JAMA.

The CDC report assessed the current risk to the US and worldwide public as low but said it could be higher for people who are exposed to infected birds on the job or through recreational activities. The report also stressed the importance of comprehensive surveillance and other preparedness efforts to keep up with a widespread pathogen that, like all influenza viruses, has the ability to evolve quickly.

Uyeki said that although the current public health risk is low, “there is cause for concern and definitely a need to be vigilant.” One concern, he said, would be if the virus established itself in mammalian hosts. So far there isn’t evidence of this, he noted.
Infections in wild land mammals—including nearly 200 animals in the US—have been sporadic, with no evidence of mammal-to-mammal transmission. Outbreaks reported in animals farmed for fur, such as mink in Spain and foxes in Finland, are unsurprising considering their densely packed living conditions, Uyeki said, and generally can be contained by culling the animals. Marine mammals that have tested positive for the virus could have been infected by contaminated feces or sea water rather than by each other, he noted.

Some mammal-to-mammal transmission may have occurred, Uyeki said. “But the real question is, is the virus continuing to infect? Is there sustained transmission in these mammals, particularly that’s not killing all of them? We’re not hearing about that.”

Monitoring and More

This spring, Runstadler and colleagues published a study in Emerging Infectious Diseases reporting H5N1 virus spillover into New England harbor and gray seals found stranded off the coast of Maine in June and July of 2022. The data did not support seal-to-seal transmission as the main route of infection, and Runstadler and his coauthors concluded that the seals were likely infected “through environmental transmission of shed virus.”

More recently, Peru reported nearly 3500 dead sea lions affected by avian influenza off the country’s coast this March. And in May, Chile reported the deaths of 9420 marine mammals infected with the virus, including more than 8000 sea lions and more than 1000 Humboldt penguins.

“For the most part, I think this is still bird to mammal [transmission], but it is very difficult to discern in the short-term,” Runstadler wrote in his email. “The number of different marine mammal infections is cause for concern,” he added, “and certainly if we detected sustained die-off or transmission in these hosts, it would be of greater concern.”

Certain genetic adaptations would be even more concerning, Uyeki said. To pose a major public health threat, “the virus probably needs to be able to bind better to receptors in the human upper respiratory tract,” he explained. So far, detailed analyses conducted worldwide of H5N1 viruses in infected wild birds, poultry, different species of terrestrial and marine mammals, and humans have not turned up signals that the virus has changed to be able to infect people more efficiently, he said.

“But,” he added, “because of the widespread geographic prevalence in wild birds and spillover to different mammals, there really needs to be increased emphasis on ongoing monitoring of these viruses.” That monitoring should include pigs, which Uyeki explained have a similar distribution of influenza virus receptors in their upper respiratory tract as humans. “I would be very concerned if highly pathogenic H5N1 viruses became established among pigs,” he said.

Beyond strengthening influenza surveillance, the WHO and its partners say nations should enhance biosecurity in farms and poultry processing facilities, apply good hygiene practices, and consider vaccinating poultry. Nations should also report and control animal outbreaks, conduct epidemiological and virological investigations around infections and outbreaks, and share virus genetic sequence data, among other measures.

As Runstadler put it, “This is an evolving situation that requires global attention and surveillance support as long as it exists.”

People likely have low immunity to the hemagglutinin protein on the surface of influenza A(H5) clade 2.3.4.4b viruses, according to the recent situation analysis. But currently available antivirals have activity against these viruses and are expected to be effective—there’s little evidence of changes to the virus associated with resistance to neuraminidase inhibitors, such as oseltamivir, or endonuclease inhibitors, such as baloxavir. The key, Uyeki said, is early initiation of antiviral treatment shortly after symptom onset, based upon observational studies of patients in the past with H5N1 infection. Moreover, the WHO has coordinated the production of a library of H5 candidate vaccine viruses, including 2 that encode a hemagglutinin protein that is identical or nearly identical to that of the dominant A(H5N1) clade.

Uyeki said clinicians should be aware that although the current risk to humans is low, that could change. For patients with respiratory disease, particularly pneumonia, clinicians could ask whether in the last week to 10 days they were closely exposed to sick or dead wild birds, poultry, or other animals, especially while not wearing a face mask. “Particularly for clinicians who are caring for patients who are hospitalized with severe pneumonia,” he said, “H5N1 should be in the differential diagnosis and influenza testing should be done in those patients.”

Published Online: July 26, 2023.

Conflict of Interest Disclosures: Dr Runstadler reported receiving funding for work related to this topic from the US Department of Agriculture, the US National Institutes of Health, and internal funding sources at Tufts University. No other disclosures were reported.

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