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Bird Flu Outbreak in Dairy Cows Is Widespread, Raising Public Health Concerns

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he ongoing global avian influenza outbreak that began in 2020 has now spread widely to US dairy cows in multiple states and is raising concerns about risks to people.

To date, the cattle outbreak has been linked with an infection in 1 person, a dairy farm worker in Texas with conjunctivitis who has since recovered. This is the first report of the highly pathogenic avian influenza (HPAI) A(H5N1) virus likely transmitting from a mammal to a human.

A new report on the dairy worker's case by Tim Uyeki, MD, MPH, MPP, chief medical officer of the Centers for Disease Control and

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Prevention (CDC) influenza division, and colleagues says it's not clear how

the person acquired the infection—whether it was by touching the eye with contaminated hands or via respiratory exposure. The person was prescribed oral oseltamivir (Tamiflu) and recovered within days without developing respiratory symptoms, according to the report.

Genome sequencing of the patient's specimen found it had no markers associated with reduced response to available influenza antivirals. Its hemagglutinin gene did not have changes that would promote its binding to receptors in the human respiratory tract or its risk of transmission in people, and it was closely related to 2 existing candidate vaccine viruses that could be used to manufacture vaccines. However, the virus did have a genetic change that has previously been associated with adaptation to mammals, the report noted.

A preprint report coauthored by researchers at the US Department of Agriculture (USDA) indicates that the virus has been circulating in cows since early December of last year, when it passed from wild birds to a single herd of cattle in Texas. As of May 2, 36 herds had been affected in 9 states, and testing found that 1 in 5 retail milk samples analyzed were positive for the virus. The virus also transmitted from cattle to other



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mammals—several barnyard cats and a raccoon—as well as to poultry and wild birds, according to the USDA report, which has not yet been peer reviewed.

The outbreak in dairy cows has surprised scientists. There have been possible contacts between cattle and HPAI H5 subtype viruses for many years, notes Martin Beer, DVM, who heads the Institute of Diagnostic Virology within the Friedrich-Loeffler-Institut, the Federal Research Institute for Animal Health, in Germany. "But there has never been a situation like this," he said in email.

Beer and colleagues previously found that cattle are not highly susceptible to the H5N1 virus.

"[T]herefore something special has to happen to allow virus circulation in cattle," he said in an email. "In the current situation, this appears to have been achieved by infection of the mammary gland. This organ system seems to act as a bioreactor and therefore further spread is possible through untreated milk and milking equipment."

A new study found that both duck and human influenza A virus receptors are widely expressed in the mammary glands of cows. Not only could this explain the high levels of H5N1 virus found in infected cows' milk, but it suggests that "cattle have the potential to act as a mixing vessel" for new influenza A viruses, the authors wrote in their preprint article, which also hasn't been peer reviewed.

For now, US and international health officials say the risk to the general public remains low but that the situation requires close surveillance and increased preparedness.

"This continued expansion in mammalian species, plus closer to our food source, means that this is the time for action," said Nahid Bhadelia, MD, MALD, director of the Boston University Center on Emerging Infectious Diseases.

What's Known About the Outbreak in Cows?

Influenza A virus was detected in milk and nasal swabs from cattle in Texas earlier this year, when veterinarians noticed that lactating cows were producing less milk and feeding less. After receiving confirmation that the animals were infected with H5N1 clade 2.3.4.4b, the same type circulating locally in birds, the USDA reported a multistate outbreak in dairy cattle on March 25 and said that it, the CDC, the US Food and Drug Administration (FDA), and state officials were investigating illness in dairy cows in Texas, Kansas, and New Mexico.

Infected herds have now been identified in those states as well as in Colorado, Idaho, Michigan, North Carolina, Ohio, and South Dakota. (Kid goats on a farm in Minnesota also tested positive in March in an outbreak unrelated to dairy cows.)

Among the key findings in the new USDA preprint report, the virus apparently transmitted in a single spillover event from wild birds to a herd of dairy cattle and then spread to different herds over 4 months before the outbreak was confirmed. Infected cows may shed the virus for 2 to 3 weeks, and cattle that were asymptomatically infected likely played a role in transmitting the virus to different herds. Worryingly, the same strain of the virus has been found in dairy cows with no connection to herds known to be infected, a finding that suggests "there are affected herds that have not yet been identified," the authors wrote.

The illness in cows is relatively mild, according to the USDA, and tends to resolve in about a week. Unlike some infected mammals identified over the past 2 years, cows with H5N1 infection don't appear to have neurological symptoms, said Jonathan Runstadler, DVM, PhD, a professor and chair of the Department of Infectious Disease and Global Health at Tufts University's Cummings School of Veterinary Medicine.

The USDA has confirmed that cow-tocow transmission occurred but says that it's still not known how the virus is spreading between the animals. The agency says high levels of the virus have not been found in respiratory samples from cows, which suggests that respiratory transmission is not a major mode.

"This is the moment where we have to figure out how transmission is happening on the farms," Bhadelia said, "and for that we need a lot more samples."

Infected cows' milk contains high titers of H5N1 virus and could be involved in transmission.

"One thing the virus does appear to be doing well is replicating in the mammary gland," said Runstadler. Mildly symptomatic infection coupled with high concentration in milk could have allowed the virus to spread undetected in dairy cows for some time, he noted.

In an effort to stop the spread in livestock, the USDA is now requiring cattle that are producing milk to be tested for influenza A virus at an approved laboratory before being moved across state lines. Positive results must be reported to the USDA. The agency is also recommending that all dairy cattle that are moved should be isolated and observed for 30 days after reaching their destination.

Preventing the virus from becoming endemic in cattle is paramount. Beer warns that the virus' high replication rates in the mammary gland and its very high titers in milk provide opportunities for further adaptation to cattle and for continued spread to other species, including mammals and humans.

The virus's establishment in cattle "must be prevented," Beer said.

Is the Milk Supply Safe? What About Beef?

On April 25, the FDA announced that its ongoing analysis involving a set of nationally representative retail cow's milk samples found that 1 in 5 were positive for H5N1 virus based on polymerase chain reaction (PCR) testing.

Then, on April 26 and May 1, the agency released preliminary results of "goldstandard" egg inoculation tests to confirm that pasteurization effectively deactivates the H5N1 virus in bovine milk, which has never before been directly examined. No live, infectious virus was detected in the 297 retail samples—including milk, cottage cheese, and sour cream—that were PCRpositive for H5N1. Samples of powdered infant formula and powdered milk products sold as "toddler formula" were all PCRnegative for H5N1, the agency said.

Based on the current evidence, the FDA says the US milk supply is safe. The agency is also testing pooled raw milk to detect how much virus is present that would need to be killed by pasteurization.

The FDA, the World Health Organization (WHO), and the Food and Agriculture Organization of the United Nations are reiterating their recommendations against consuming raw milk, which hasn't undergone pasteurization. Runstadler said he would be particularly concerned about drinking raw milk or eating raw milk products during the current outbreak in dairy cows. "People who consume those are potentially consuming infectious doses of the virus," he said.

Meanwhile, the USDA is also testing beef. Thirty retail ground beef samples from states with infected dairy cattle herds were negative for H5N1 on PCR testing, according to a May 1 update.

Is Bird Flu Currently a Risk to People?

It's important to note that the term *highly pathogenic* avian influenza refers to sickness in birds, not necessarily humans. The current global bird flu outbreak has caused sporadic infections in people, some of them serious. Since 2022, 26 H5N1 cases have been reported in people in 8 countries, nearly all after exposure to sick or dead poultry. Fourteen of those cases were severe or critical, and 7 people died.

Two of the milder cases were in the US. Before the Texas dairy farm worker, a case was confirmed in 2022 in a poultry worker in Colorado, who also quickly recovered.

According to the CDC, people who have been exposed to infected cattle are being monitored for 10 days. Since this March, at least 220 people have been monitored and at least 30 have been tested. Only 1 known positive case, in the dairy farm worker, has been associated with the cattle outbreak so far.

For now, both the CDC and the WHO alongside other international groups say the current risk to the general public is still low. The CDC is conducting ongoing surveillance for signals of unusual flu activity in emergency departments and public health and clinical laboratory test results. Wastewater surveillance is also under way, but results haven't been fully reported yet.

No uptick in flu activity was detected for the week that ended April 27, according to the CDC. Bhadelia cautioned, however, that some workers who are sick may not come forward for testing for fear of losing employment and that this could obscure additional cases. Occupational health records from the last few months might provide some insight, she said.

"If one person on a farm got this infection and these infections are a lot more widespread than we thought among cows, then my gut tells me there's probably a lot more human infections we have not detected," said Bhadelia, who was formerly the White House's senior policy advisor for Global COVID Response.

People who may come into contact with infected mammals or birds, either recreationally or at work, are at greater risk of infection. The CDC is providing interim safety recommendations for poultry and livestock farmers and workers, slaughterhouse workers who handle lactating dairy cattle, owners of backyard bird flocks, veterinarians and their staff, and public health or animal health responders. A new 1-sheet resource available in English and Spanish describes the recommended personal protective equipment-including gloves, an approved respirator, and safety goggles or a face shield-and donning and doffing procedures for people working "with sick or dead animals, animal feces, litter, raw milk, and other materials that might have the virus."

The CDC and international agencies have said they expect that people will be sporadically infected as long as the virus is circulating widely. According to the CDC website, "[c]linicians should consider the possibility of HPAI A(H5N1) virus infection in persons showing signs or symptoms of acute respiratory illness who have relevant exposure history."

"If you take care of someone who works in the dairy industry you need to be alert," Carlos del Rio, MD, a professor of medicine at Emory University School of Medicine and immediate past president of the Infectious Diseases Society of America, said in an email.

How Does the Dairy Cattle Outbreak Affect Public Health Risk?

Beyond the immediate risk, Bhadelia and other experts say the virus' ongoing spread in mammals could have public health implications. "Once considered primarily a threat to poultry," the World Organisation for Animal Health warned in a March 13 statement, now the virus "is moving from wild birds to wild mammals with impacts beyond anything previously seen."

Since 2021, H5N1 viruses have been detected in 37 new mammal species worldwide, the organization says. This includes nearly 20 species of wild mammals in 28 US states since 2022, according to the USDA's Animal and Plant Health Inspection Service. Globally, as of this past December, bird flu has reached mammals on both the north and south poles—a polar bear in the Arctic and seals in the Antarctic. And in some cases, as with farmed mink in 2022 and now dairy cows, mammal-to-mammal transmission has occurred.

Experts say all this passing around of the virus presents more chances for it to become better suited to replicate and transmit in mammals, with potentially grave consequences.

"Vigilance is needed because if HPAI A(H5N1) virus adapts and becomes established among cows or other mammals, the risk to public health may increase," the authors of the dairy farm worker's case report wrote in a supplementary appendix.

Because the virus has already jumped into cows and then to other animals, one concern is that it could make its way into other livestock, namely pigs. Unlike cows, pigs harbor other influenza A viruses, some of which are already adapted to humans, Beer explained. If these viruses exchanged genes with H5N1, a more zoonotic strain or even a pandemic strain could potentially emerge. "Therefore, to prevent further adaptation or reassortment in pigs, transmission to pigs should also be prevented," Beer said. According to Bhadelia, the USDA says it is conducting surveillance in pigs and hasn't found anything yet.

Could proactive surveillance have caught the cattle outbreak earlier? "You can't do anything surveillance-wise that's completely covering everything," Runstadler. "But I think it's worth considering, given what this virus has been doing in the last couple of years in particular, and its spread globally and its spill into different species, whether a good plan would be to do more proactive surveillance in both agricultural and wild animal species..."

Runstadler, who has investigated H5N1 avian influenza infections in marine mammals, noted the virus is continuing to circulate in wild birds, causing waves of infection and death. He pointed to a minor outbreak that has killed birds in the northeast US over the past several weeks after a lull in activity. "There's every indication that that's continuing to happen, and we should expect that to continue to happen until the virus does something new."

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Note: Source references are available through embedded hyperlinks in the article text online.