# A second US farmworker infected with the bird flu virus

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The Michigan Department of Health and Human Services (MDHHS) issued an alert on Wednesday stating they had identified a farmworker infected with the same bird flu virus that has been infecting livestock across several states in the US.

This is the second confirmed case related to the H5N1 outbreak among dairy cows and the second known mammal to human transmission. Health authorities indicated that the infected person has since made a full recovery. The MDHHS added, “To protect farm and farmworker privacy, additional details are not being provided.”

The Centers for Disease Control and Prevention (CDC) also issued a report noting that the swab from the Michigan patient’s eyes confirmed the presence of the virus. Like the Texas animal handler, his only symptoms consisted of conjunctivitis or inflammation of the eyes. Although the swab from the Michigan farmworker was negative, it was positive in the case from Texas.

Dr. Natasha Bagdasarian, Chief Medical Executive for the State of Michigan and board certified in infectious disease, explained the case was detected in part from state efforts to monitor workers from farms that have infected herds. She noted, “Michigan has really been one of the states leading in terms of testing. So, it’s not surprising that we have picked up on this sporadic case.”

Bagdasarian reiterated the assurances that have been made since late March when the outbreak among dairy cows had been detected: “The current health risk to the general public remains low. This virus is being closely monitored, and we have not seen signs of sustained human-to-human transmission at this point. This is exactly how public health is meant to work, in early detection and monitoring of new and emerging illnesses.”

At Wednesday’s news briefing, Dr. Nirav Shah, the CDC’s principal deputy director, conveyed that the negative nasal swab is reassuring: “It reduced the likelihood—it does not eliminate, but it reduces the likelihood—of a respiratory route of transmission.”

The leading hypothesis for these two infections is thought to be direct transmission. Given the high viral load in infected dairy cow milk, handling of the animals and the equipment used can have easily contaminated the hands and clothes of workers and transferred the particles directly into their eyes and nostrils. Other considerations include cleaning with sprays that cause the virus to aerosolize and then seed on the faces of workers.

According to the US Department of Agriculture’s (USDA) Animal and Plant Health Inspection Services, the number of herds impacted has risen to 52 across nine states in the US. Given the reluctance on the part of farmers to allow their animals and workers to be tested out of fear of the stigma associated with the epidemic, experts believe that the number of people potentially infected is far higher.

Currently, serological surveys remain to be done to provide an honest appraisal of the scope of the zoonotic spillover into farmworkers and the surrounding communities. Bagdasarian admitted, “We’ve always talked about the need to do additional studies … and to do a big look at serology, especially for people who may have remained asymptomatic throughout. That would be a next step.” Shah also agreed that “at this time, we’re not there yet.”

Gregory Gray, an epidemiologist at the University of Texas Medical Branch in Galveston who has had decades of experience in studying respiratory infections among animal handlers, including dairy cattle,

told NPR, “We know that some of the workers sought medical care for influenza-like illness and conjunctivitis at the same time the H5N1 was ravaging the dairy farms, I don’t have a way to measure that, but it seems biologically quite plausible that they too are suffering from the virus.”

On the question of what is required for this virus to acquire the correct sequence of mutations to evolve into a pathogen that is easily transmitted between people, virology and infectious disease experts weighed in with their replies in an important report published in the journal *Science*.

Fundamentally, famed virologist Martin Beer of the Friedrich Loeffler Institute, said, “This clade [2.3.4.4b] is most of all and more than all previous clades an avian virus.” He has not seen signs in his lab that the virus can efficiently infect human cells.

Over a decade ago, important work by Mathilde Richard at Erasmus Medical Center, who was working with H5N1 and ferrets, was halted out of concerns raised by issues surrounding gain of function experiments. It was precisely the very same evolutionary mutations that researchers are seeing taking place that are leading to a wider array of animals becoming susceptible to H5N1 infections. As she noted, “I do think that this has really, really slowed down our knowledge.”

Scientists have since had to rely on tracking epidemics among mammals, sequencing the viruses and assessing the mutations acquired that allow the new strains their capabilities. Richard told *Science*, “That is sort of like a massive gain-of-function experiment in nature, and from those outbreaks, you can still learn quite a lot.”

The first step that virologists have identified is the ability of the virus to borrow the host proteins that can replicate its RNA genome. One known mutation of these PB2 proteins, E627K, was first seen in the avian flu that caused the 1918 pandemic. Tom Peacock, virologist at the Imperial College London, said, “PB2 was so good that it has stuck in every human influenza virus until the 2009 swine flu pandemic.” The E627K mutations have been found in samples obtained from infected foxes and seals during the current global bird pandemic.

Peacock then notes that hemagglutinin (HA), the virus protein that helps the virus attach to the host cells, has to change sufficiently to allow for an efficient binding. He said, “That is absolutely essential. In fact, there are no influenza viruses that are transmissible between people that don’t have a human-adapted hemagglutinin.”

The third mutation, said Emory University virologist Seema Lakdawala, who is also an expert in airborne transmission of pathogens, is a mutation that can stabilize the virus's HA proteins in small droplets of moisture that allows it to become transmissible through air. Lastly, Beer postulated that the other challenge remaining for the virus is the ability to evade the immune system. Further research by Lakdawala is looking into how likely it would be for these novel viruses to emerge in the context of pre-existing immunity to seasonal influenza.

As Peacock observed, H5N1 “has one of the highest barriers to becoming a pandemic virus of any avian influenza virus. It’s really wrong in so many ways. But obviously it only has to get the right combination of mutations once to do the jump.” In the context of the ongoing sustained pandemic among birds, Richards went further: “This is the threat that’s going to keep knocking at our door until it will indeed, I assume, cause a pandemic. Because there is no way back.”

Several projects on these issues are currently getting underway. Earlier this month, *Science* reported samples of H5N1 from Cornell University were sent to the German Federal Research Institute for Animal Health on the isle of Riems, which contains high-security labs equipped to study the impact of these pathogens in large animals. According to Beer, the initial study will infect dairy cows to get a “fuller picture” of the dangers posed by the virus. Additional work will include understanding how the virus is transmitted among the animals.

As Beer remarked, “Nobody wants this dangerous virus to become entrenched in a new species that we use to produce food and that has so much close contact to humans.”