

Health

H5N1 bird flu is closer to gaining pandemic potential than we thought

The flu virus currently circulating in birds and dairy cows is already better at infecting people than earlier variants, and a single mutation would allow it to bind to key human receptors

By Michael Le Page

5 December 2024



A highly infectious strain of bird flu has been circulating worldwide since 2020

The H5N1 [bird flu](#) virus that has spread worldwide is already [better at infecting people](#) than earlier strains. What's more, a single mutation could allow it to infect the cells lining our noses and throats, making it more likely to go airborne.

This change alone is not enough for the virus to be capable of causing a pandemic. However, if a virus with this mutation swapped genes with a human flu virus, it could acquire pandemic potential almost instantly.

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"The more people get infected, the more likely it is that something like this could arise," says [Ian Wilson](#) at the Scripps Research Institute in California. Despite this, Wilson thinks the risk remains low.

A particularly virulent form of H5N1 bird flu evolved in the 1990s, probably in domestic birds in China, and spread worldwide. Around 2020, a new variant of this virus emerged and spread even more widely, reaching the Americas and [Antarctica](#). It has infected domestic poultry in large numbers and is also [spreading among dairy cows in the US](#), causing occasional human cases.

A team led by [Debby van Riel](#) at the Erasmus University Medical Center in the Netherlands has now infected human nose and throat cells with H5N1 variants from 2005 and 2022. They have shown for the first time that the 2022 variant is better at binding to these cells and also better at replicating inside them. "It's bad news," says van Riel.

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"I don't think the chances of the virus becoming pandemic are extremely high," she says. But the fact that the virus is better at infecting humans will give it more opportunities to acquire additional mutations that increase its pandemic potential.

Meanwhile, Wilson and his colleagues have been studying the crucial haemagglutinin protein of the flu virus. This protein binds to receptors on the outside of cells, determining which cells the virus can infect. Because it protrudes from the virus, it is also the main target of the immune system.

At present, the H5N1 haemagglutinin binds mainly to receptors that in humans are found deep in the lungs. This means it can cause severe disease but it is unlikely to get out of the body and infect others. To do that, the virus needs to infect cells lining the nose and throat, meaning viruses can be coughed or sneezed out to infect others.

Van Riel's study suggests the virus can do this to some degree, but it's not clear whether the virus is binding to the main receptors on these cells. It was thought that multiple mutations would be required for H5N1 to bind strongly to these receptors, but Wilson's team has now shown that with the current H5N1 variant, a single mutation is all it would take.



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Neuroscientists have been surprised to discover that the human brain is teeming with microbes, and we are beginning to suspect they could play a role in neurodegenerative disorders like Alzheimer's

This change alone would not result in a virus capable of going pandemic, says team member [Jim Paulson](#), also at the Scripps Research Institute. "We view this property as required – but importantly not sufficient – for transmission, for a pandemic virus," he says.

Other changes are also necessary for the virus to start to replicate and spread from person to person, says Paulson, and these are not well understood. "There's a lot of biology that we don't even know," he says.

Once an H5N1 virus infecting a human acquired the receptor-switching mutation, however, it would then have a chance of evolving these other changes as well.

What's more, in theory, it could acquire all the abilities it needs in one fell swoop by swapping genes with a human virus infecting the same individual. Several [previous flu pandemics were caused by animal and human flu viruses swapping genes](#), says Paulson.

"This is highly concerning," says [Aris Katzourakis](#) at the University of Oxford, who was not involved in either study. "Each spillover to a human gives the virus a roll of the dice."

How deadly would an H5N1 pandemic be?

If H5N1 bird flu does manage to start spreading from person to person, the big question is how deadly it would be. Of the people confirmed to be infected with the virus since 2003, half have died. However, the true infection fatality rate could be lower as many cases have probably gone undetected, and [milder ones are more likely to be missed](#).

Among the 60 or so people infected in the US since the dairy outbreak began, almost all have had mild symptoms only. Why is [not understood](#), but one explanation is that many were infected via the eyes. "That is known to have far milder outcomes," says Katzourakis.



We are finally starting to understand brain fog and how to treat it

Brain fog – which encompasses memory problems, lack of mental clarity and an inability to focus – had eluded scientific scrutiny until covid-19 thrust it into the spotlight. Now, we're starting to learn more about what exactly it is and how we can beat it

It is also thought that when viruses switch from binding to receptors deep in the lungs to those higher in the respiratory tract, they become less dangerous. But the puzzling aspects of the cases in the US have left Paulson unsure that this will hold true with H5N1. "Now I just don't know what to think, to be honest," he says.

"I don't think there is any reason to be complacent in this respect, and anticipate 'mildness' should this virus become readily human-to-human transmissible," says Katzourakis.

Wilson's team studied the haemagglutinin protein in isolation, so there was no chance of a lab leak of the mutant protein. "There was no virus used at all here," he says.

Reference: [bioRxiv DOI: 10.1101/2024.11.27.625596](#)

Journal reference: [Science DOI: 10.1126/science.adt0180](#)

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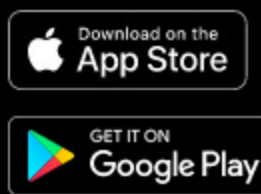
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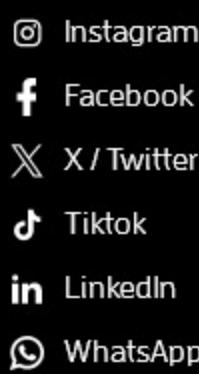
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