

Study Identifies Influenza Viruses Circulating In Pigs And Birds That Could Pose A Risk To Humans

In the summer of 1968, a new strain of [influenza](#) appeared in Hong Kong. This strain, known as H3N2, spread around the globe and eventually killed an estimated 1 million people.

A new study from MIT reveals that there are many strains of H3N2 circulating in birds and pigs that are genetically similar to the 1968 strain and have the potential to generate a pandemic if they leap to humans. The researchers, led by Ram Sasisekharan, the Alfred H. Caspary Professor of Biological Engineering at MIT, also found that current [flu](#) vaccines might not offer protection against these strains.

"There are indeed examples of H3N2 that we need to be concerned about," says Sasisekharan, who is also a member of MIT's Koch Institute for Integrative Cancer Research. "From a pandemic-preparedness point of view, we should potentially start including some of these H3 strains as part of influenza vaccines."

The study, which appears in the May 10 issue of the journal *Scientific Reports*, also offers the World Health Organization and public-health agencies' insight into viral strains that should raise red flags if detected.

Influenza evolution

In the past 100 years, influenza viruses that emerged from pigs or birds have caused several notable flu pandemics. When one of these avian or swine viruses gains the ability to infect humans, it can often evade the immune system, which is primed to recognize only strains that commonly infect humans.

Strains of H3N2 have been circulating in humans since the 1968 pandemic, but they have evolved to a less dangerous form that produces a nasty seasonal flu. However, H3N2 strains are also circulating in pigs and birds.

Sasisekharan and his colleagues wanted to determine the risk of H3N2 strains re-emerging in humans, whose immune systems would no longer recognize the more dangerous forms of H3N2. This type of event has a recent precedent: In 2009, a strain of [H1N1](#) emerged that was very similar to the virus that caused a 1918 pandemic that killed 50 million to 100 million people.

"We asked if that could happen with H3," Sasisekharan says. "You would think it's more readily possible with H3 because we observe that there seems to be a lot more mixing of H3 between humans and swine."

Genetic similarities

In the new study, the researchers compared the 1968 H3N2 strain and about 1,100 H3 strains now circulating in pigs and birds, focusing on the gene that codes for the viral hemagglutinin (HA) protein.

After comparing HA genetic sequences in five key locations that control the viruses' interactions with infected hosts, the researchers calculated an "antigenic index" for each strain. This value indicates the percentage of these genetic regions identical to those of the 1968 pandemic strain and helps determine how well an influenza virus can evade a host's immune response.

The researchers also took into account the patterns of attachment of the HA protein to sugar molecules called glycans. The virus' ability to attach to glycan receptors found on human respiratory-tract cells is key to infecting humans.

Seeking viruses with an antigenic index of at least 49 percent and glycan-attachment patterns identical to those of the 1968 virus, the research team identified 581 H3 viruses isolated since 2000 that could potentially cause a pandemic. Of these, 549 came from birds and 32 from pigs.

The researchers then exposed some of these strains to antibodies provoked by the current H3 seasonal-flu vaccines. As they predicted, these antibodies were unable to recognize or attack these H3 strains. Of the 581 HA sequences, six swine strains already contain the standard HA mutations necessary for human adaptation, and are thus capable of entering the human population either directly or via genetic reassortment, Sasisekharan says.

"One of the amazing things about the influenza virus is its ability to grab genes from different pools," he says. "There could be viral genes that mix among pigs, or between birds and pigs."

Sasisekharan and colleagues are now doing a similar genetic study of H5 influenza strains. The H3 study was funded by the National Institutes of Health and the National Science Foundation.

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