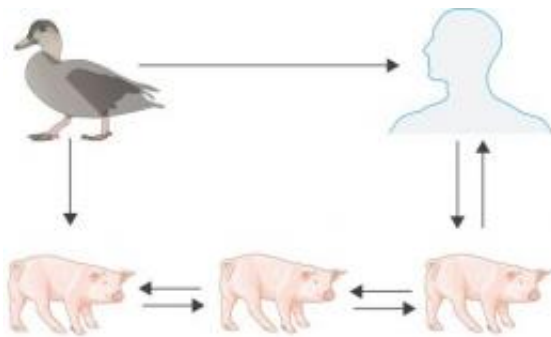# Long-term study of swine flu viruses shows increasing viral diversity

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The gene flow of influenza A viruses occurs among birds, pigs and humans.

Increased transportation of live pigs appears to have driven an increase in the diversity of swine influenza viruses found in the animals in Hong Kong over the last three decades, according to a new study.

In the longest study of its kind, Duke-NUS Graduate Medical School researchers found that swine viruses crossed geographic borders and mixed with local viruses, increasing their diversity.

"The majority of reported human infections have been people with close contact to farm animals," said Vijaykrishna Dhanasekaran, Ph.D., an assistant professor at Duke-NUS, who works in the Laboratory of Virus Evolution.

"I think the risk of swine-to-human transmission has not increased greatly, but the diversity of swine viruses has increased as shown in our study," Vijaykrishna said. "This means that the repertoire of viruses that humans are in contact with everyday has increased and this may lead to a higher likelihood of swine-to-human transmission, although the risk remains unquantified."

The study was published online in the journal *Nature* on May 25.

"The geographic transport of swine viruses that we highlight in our study is likely through the transport of live pigs," Vijaykrishna said. "Most swine viruses that have been described to date have been isolated from farmed pigs in Asia, Europe and North America. Some viruses have been isolated from backyard pigs in southeast Asia. However, no information is available on status of influenza in naturally roaming wild or domestic pigs."

The study looked at the epidemiology, genetics and antigenic properties of swine influenza virus in Hong Kong from more than 650 samples taken from swine, more than 800 swine blood specimens from 12 years of surveillance, and 34 years worth of other data on swine flu viruses. Antigens are the features on the surface of the virus that pigs and humans develop antibodies against to fight the infection. Influenza viruses evade the immune response by mutations in the hemagglutinin protein, an attachment protein that serves as an antigen. Antibodies formed during previous infections fail to recognize the newly mutated antigen, which is why seasonal influenza vaccines have to be reformulated each year.

Mutations in the swine influenza hemagglutinin have been linked to reassortment, which is the mixing of genetic material from multiple virus species into new combinations, said Vijaykrishna. The greater viral diversity they found in the swine flu viruses may mean more possible

combinations from reassortment.

"These results provide important clues into the mechanism of influenza virus evolution in general," he said.

The researchers discovered that two major lineages of H1 subtype viruses and the human H3N2 viruses were frequently detected in swine. Several combinations of the three lineages were detected in pigs, including some avian (bird) viruses.

While the pigs had no symptoms or very mild undetected symptoms to most viruses isolated for the study, the scientists don't know how virulent these viruses can be in humans. "It is important to monitor viruses in swine, especially those that can emerge in humans that we do not have antibodies for," said Vijaykrishna, who is a faculty member of the Duke-NUS Program on Emerging Infectious Diseases.

  More information: D Vijaykrishna et al. Long-term evolution and transmission dynamics of swine influenza A virus. *Nature* DOI:10.1038/nature10004 (2011).

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