

Flu viruses take one-way ticket out of Asia, then travel the world

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Seasonal influenza strains constantly evolve in overlapping epidemics in Asia and sweep the rest of the world each year, an international research team has found.

These findings suggest that by focusing surveillance efforts on East and Southeast Asia, researchers may be able to extend their forecast of the flu strains most likely to cause epidemics, which may in turn help experts decide which strains should go in the flu vaccine each year.

The study, by a team of researchers from Europe, Australia, Japan and the United States, appears in the 18 April issue of the journal *Science*, which is published by AAAS, the nonprofit science society.

“The flu virus is constantly mutating, so it’s a major challenge for public health as well as a fascinating example of evolution in action. This study advances our knowledge of how new flu strains spread across the globe and how epidemics arise,” said Katrina Kelner, *Science*’s deputy managing editor, life sciences.

Colin Russell of the University of Cambridge in the United Kingdom and his colleagues analyzed 13,000 samples of influenza A (H3N2) virus, collected across six continents from 2002 to 2007 by the World Health Organization Global Influenza Surveillance Network. This subtype of influenza is currently the major cause of flu-related illness and death in humans.

The researchers compared physical differences in a surface protein, called hemagglutinin, across the different samples. Hemagglutinin is the primary target of the immune response, and even small changes can allow the virus to evade the immune system and cause disease.

In a subset of the samples, the researchers also compared the sequences of the gene that codes for hemagglutinin.

Together, these analyses allowed the researchers to identify different strains of A (H3N2) as they arrived at new locations around the world over the five-year period. The results revealed that strains emerge in East and Southeast Asia and then about six to nine months later reach Europe and North America. Several months later still, the strains arrive in South America. Essentially, once the strains leave East and Southeast Asia they enter an evolutionary graveyard.

“The ultimate goal of our collaboration is to increase our ability to predict the evolution of influenza viruses. This study is one step along that path and in particular highlights the importance of ongoing collaborations and surveillance in East and Southeast Asia, and of expanding these collaborations in the future,” said Derek Smith of the University of Cambridge, who is the corresponding author of the study.

Annual influenza epidemics are thought to result in 3 to 5 million cases of severe illness, and between 250,000 and 500,000 deaths every year, according to the World Health Organization (<http://www.who.int/mediacentre/factsheets/fs211/en/index.html>).

A (H3N2) is a subtype of the influenza A virus, and it is one of the three flu viruses included – in dead or in a weakened state – in the flu vaccine. The others are the influenza A (H1N1) subtype and the influenza B virus. Each year, the World Health Organization decides which strains within these three categories to include in the next vaccine, based on the

recent activity of strains that are currently circulation.

The authors emphasized that the flu vaccine currently works extremely well, protecting about 300 million people from the disease each year, and that people should continue to be vaccinated annually. But, from time to time, a new strain begins infecting people after the vaccine has already been produced.

For decades, researchers haven't known how influenza viruses migrate around the world. According to some of the scenarios that have been proposed, the viruses may migrate between the Northern and Southern hemispheres following the seasons, or they may have come out of the tropics where they were thought to circulate continuously, or they may have come out of China.

The *Science* study shows instead that each year since 2002, influenza A (H3N2) viruses have migrated out of what the authors call the "East and Southeast Asian circulation network," and from there spread around the world.

Why Asia? For reasons that aren't well-understood, flu epidemics break out during the rainy seasons in the tropics of East and Southeast Asia. On continents at higher latitudes, on the other hand, flu season simply occurs for a few months during the wintertime. Within Asia, different regions experience the rainy season at different times of year.

"Flu epidemics appear to be driven by seasonal factors such as winter, or rainy seasons. So there can be cities that are only 700 miles away from each other, such as Bangkok and Kuala Lumpur, which have epidemics six months apart. There is a lot of variability like this in East and Southeast Asia, so lots of opportunity for an epidemic in one country to seed an epidemic to another nearby country, like a baton passed by runners in a relay race," Smith said.

“Our study is an example of the tremendous synergy between influenza science and public health,” he said. “The World Health Organization’s Global Influenza Surveillance Network tracks the evolution of influenza viruses for the primary purpose of influenza vaccine strain selection, but this also enables basic work on evolution.”

Source: American Association for the Advancement of Science

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