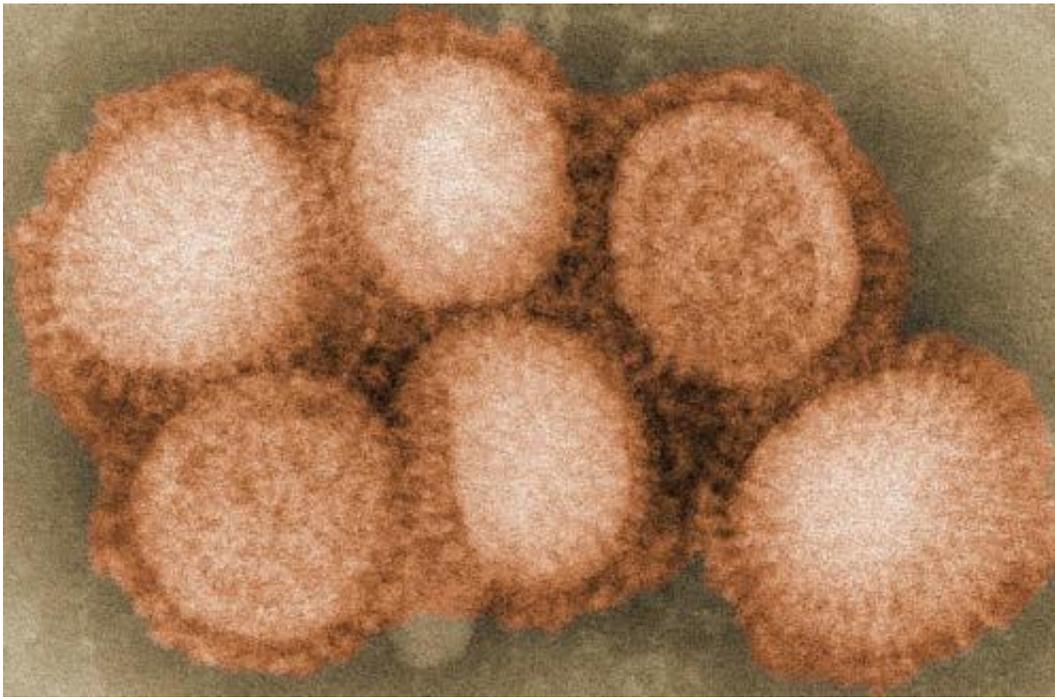


Virus evolution and human behavior shape global patterns of flu movement

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H1N1 virus. Credit: C. S. Goldsmith and A. Balish, CDC

The global movement patterns of all four seasonal influenza viruses are illustrated in research published today in the journal *Nature*, providing a detailed account of country-to-country virus spread over the last decade and revealing unexpected differences in circulation patterns between viruses.

In the study, an international team of researchers led by the University of

Cambridge and the Fred Hutchinson Cancer Research Center, and including all five World Health Organization (WHO) Influenza Collaborating Centres, report surprising differences between the various types of seasonal flu virus, which they show to be due to the rate at which the different viruses evolve.

There are four types of influenza viruses that cause seasonal flu in humans: two influenza A viruses (H3N2 and H1N1) and two influenza B viruses (Yamagata and Victoria). While H3N2 viruses are the most common of the seasonal influenza viruses, H1N1 and B viruses also cause epidemics worldwide each year, hence the WHO selects representative strains of all four A and B viruses for inclusion in the seasonal influenza vaccine each year.

Importantly, all four of the viruses cause indistinguishable symptoms and evolve by similar mechanisms to escape immunity induced by prior infections and vaccinations. This 'antigenic' evolution is part of why people get influenza multiple times over the course of their lives.

In 2008, an international team led by scientists from the University of Cambridge, writing in the journal *Science*, showed that H3N2 viruses circulate continuously in East and Southeast Asia throughout the year, spreading to the rest of the world each year to cause seasonal flu epidemics. Given the fundamental similarities between H3N2, H1N1, and B infection it was thought that they would also emerge from east and southeast Asia to cause yearly epidemics worldwide. However, the work published today in *Nature* shows that in fact, H1N1 and B viruses behave very differently from H3N2 viruses.

Senior author Dr Colin Russell, from the Department of Veterinary Medicine at the University of Cambridge, UK, says: "While H3N2 viruses die out between epidemics and new viruses emerge from east and southeast Asia every year, H1N1 and B viruses frequently circulate

continuously between epidemics worldwide. This continuous circulation gives rise to a huge diversity in H1N1 and B viruses circulating globally."

Interestingly, the researchers found that sometimes new H1N1 and B variants emerge from outside east and southeast Asia and are subsequently seeded into Asia, while in other cases H1N1 and B variants circulate in Asia for years without spreading globally.

"It's really surprising to find that the H3N2 viruses are unique among the seasonal influenza viruses," adds first author Dr Trevor Bedford from the Fred Hutchinson Cancer Research Center in Seattle, USA. "It's almost as surprising to find that the differences among viruses are associated with a simple phenomenon: how quickly the viruses evolve antigenically."

The *Nature* study finds that the rate of global movement of each virus, and its ability to circulate continuously between epidemics, is shaped by how quickly that virus changes its coat to escape immunity in the human population. Viruses that evolve quickly, in particular H3N2, spread around the world rapidly, but die out quickly between epidemics. Viruses that evolve more slowly, like H1N1 and B viruses, spread around the world more slowly but are also better at circulating continuously between epidemics.

The key element about global movement is who is getting infected: faster evolving viruses, like H3N2, can infect adults, who tend to travel more frequently than children, providing more opportunities for the virus to spread. Conversely, more slowly evolving viruses, such as H1N1 and B viruses, primarily infect children. Children get sick with all four seasonal flu viruses, but H3N2 evolves faster so it infects adults more often. This leads to a greater proportion of adult infections with H3N2 relative to H1N1 and B viruses, and faster spread of H3N2 viruses.

"Ultimately, this means that we can look at the viruses circulating in Asia to get a good idea of which H3N2 virus might spread worldwide, but for H1N1 and B it's tremendously variable and the dominant variant can vary from one region of the world to another," says Dr Russell.

The *Nature* study also sheds important light on the role of India in the global spread of seasonal influenza viruses. Scientists and public health officials had long known that China and Southeast Asia were important for the evolution and spread of [seasonal influenza](#) viruses. However, based on the analysis of an extensive collection of [viruses](#) from India, it is now clear that India may be as central as China to the ongoing evolution of seasonal [influenza viruses](#).

"The focus of influenza research in the past has been on China and southeast Asia, but it seems obvious now that surveillance and public health in India, home to over one sixth of the world's population, should be a high priority for further development to help safeguard India and the world against [seasonal flu](#)," says Dr Mandeep Chadha of the National Institute of Virology, Pune, India.

More information: Bedford, T et al. Global circulation patterns of seasonal influenza viruses vary with antigenic drift. *Nature*; 8 June 2015. [dx.doi.org/10.1038/nature14460](https://doi.org/10.1038/nature14460)

Provided by University of Cambridge

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