

THE GLOBAL EVOLUTION AND CIRCULATION OF INFLUENZA VIRUSES

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Thirty plus years of global influenza virus surveillance, in multiple species, provides a remarkable dataset for the study of influenza virus evolution. Because the purpose of much of this surveillance is vaccine strain selection, these data have been analyzed antigenically as well as genetically. I will describe a method, *antigenic cartography*, that resolves the paradoxes in, and increases the resolution of, binding assay data such as hemagglutination inhibition, virus neutralization, and ELISA data. Using this method I will describe the antigenic evolution of influenza A(H3N2) viruses from the last influenza pandemic in 1968, and an antigenic and genetic analysis of the hemagglutinin of ~13,000 influenza A(H3N2) viruses from six continents during 2002-2007. One finding of these studies is that from 2002-2007, influenza viruses did not persist in any individual country, but nevertheless continuously circulated in East and Southeast Asia (E-SE Asia) via a region-wide network of temporally overlapping epidemics. Epidemics in the rest of the world were seeded from this E-SE Asian network each year. Seed strains generally first reached Oceania, North America, and Europe, and later South America. Thus, once A(H3N2) viruses leave E-SE Asia, they are unlikely to contribute to long-term viral evolution. If the trends observed during this period are an accurate representation of overall patterns of spread, then the evolution, and thus antigenic characteristics, of A(H3N2) viruses outside E-SE Asia may be forecast each year based on surveillance within E-SE Asia. These studies of human influenza viruses will be contrasted with studies in other species, to show the importance of the coevolution of the virus and population-level immunity to the virus.